

Background

7 U.S.C. 136a provides that "[e]xcept as provided by this subchapter, no person in any State may distribute or sell to any person any pesticide that is not registered under this subchapter. To the extent necessary to prevent unreasonable adverse effects on the environment, the Administrator may by regulation limit the distribution, sale, or use in any State of any pesticide that is not registered under this subchapter and that is not the subject of an experimental use permit under section 136c of this title or an emergency exemption under section 136p of this title."

According to the BE

The proposed Federal action addressed in this Opinion (hereafter, the Action) is the registration of chlorpyrifos under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The FWS considers the duration of the Action to be 15 years, accounting for the 15-year registration cycle for FIFRA Section 3 and Section 24(c) registration, and the applicable duration for other uses for this chemical, unless otherwise specified on the product labels. The following chemical-specific descriptions are taken largely from EPA's BE for chlorpyrifos.

For this pesticide, the Action includes registration of the uses, as described by product labels, of all pesticide products containing the active ingredient, its metabolites and degradates, any other active ingredients, other ingredients within the formulations (e.g., adjuvants and inert ingredients), and any recommended tank mixtures. The Action also includes all authorizations for use of pesticide products, including the use of existing stocks, and active labels of products containing the active ingredient. A complete listing of product uses is found in the Agricultural and Non-agricultural Uses sections below.

In their BE, EPA considered the likely use types of the products over the duration of the Action, although the Agencies recognize future uses are difficult to predict with either accuracy or precision, particularly as more time passes. Thus, future uses have been addressed to the extent possible in EPA's BE where the geographic distribution and magnitude of exposure (including application rate and methods of application) have been included in the scope of the assessment. Where new uses, rate increases, or an application method that increases exposure beyond what was addressed in the BE and this Opinion are approved or proposed, re-initiation of consultation would be required.

The purpose of the Action, as noted in EPA's BE, is to provide tools for pest control on food and feed crops, as well as other non-agricultural uses that do not cause unreasonable adverse effects to the environment throughout the United States and its affiliated territories. For additional information on the registration and re-registration review processes, see section 1.1.1. of the Problem Formulation in the BE. The following sections describe the Action in greater detail, and are taken largely from EPA's BE for chlorpyrifos.

The pesticide chlorpyrifos has been used for approximately the last 50 years, and it is undergoing a 15 year re-registration by the US EPA. As described in FWS draft

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CONCLUSION

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INFORMATION/BRIEFING MEMORANDUM FOR THE SECRETARY

DATE: May 13, 2019

THROUGH: Margaret Everson, Principal Deputy Director, U. S. Fish and Wildlife Service Exercising the Authority of the Director of the U.S. Fish and Wildlife Service

FROM: Gary Frazer, Assistant Director – Ecological Services, U. S. Fish and Wildlife Service

SUBJECT: Status of ESA section 7 consultations with EPA on re-registration of 3 pesticides

I. BACKGROUND

Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the U.S. Environmental Protection Agency (EPA) is responsible for registering pesticides and ensuring that pesticides do not cause unreasonable adverse effects on the environment, which includes species listed as threatened or endangered (listed species) under the Federal Endangered Species Act (ESA). Pursuant to section 7 of the ESA, Federal agencies must, in consultation with and with the assistance of U.S. Fish and Wildlife Service (Service) and National Marine Fisheries Service (NMFS), ensure that any action authorized, funded, or carried out by such agency is not likely to jeopardize the continued existence of any listed species or result in the destruction or adverse modification of their critical habitat.

Until recently, the Service, EPA and NMFS used different risk assessment approaches to identify the potential effects of pesticides on threatened and endangered species and were unable to reach a consensus on an approach for assessing the risks to listed species. These different approaches to risk assessment impacted the ability of EPA, the Service, and NMFS to complete consultation under the ESA. As a result, several lawsuits related to noncompliance of pesticide registration with section 7 of the ESA were filed against EPA, the Service, and NMFS.

To resolve these differences, EPA, FWS, NMFS, and the United States Department of Agriculture (USDA) (collectively the agencies) asked the National Academy of

Sciences (NAS) to evaluate the differing risk assessment approaches used by the agencies to identify the potential effects of pesticides on listed species. The NAS issued a report on April 30, 2013, entitled “Assessing Risks to Endangered and Threatened Species from Pesticides.” The NAS report recommends that EPA, FWS, and NMFS take a common approach to assessing the potential effects of pesticides on listed species. The agencies are working collaboratively to implement the recommendations made in the NAS report.

Due to the complexity of these consultations, large number of species addressed (approximately 1,750 listed species and critical habitat for 650 species), and a concern regarding sustainability for future consultations, the agencies are also working towards identifying and incorporating streamlining measures, automation, and other efficiencies into the current and future consultation processes. The overarching goal of the interim approach is to collaboratively develop a practicable consultation process for future proposed pesticide registration actions that is efficient, transparent, and sustainable and meets the regulatory compliance under FIFRA and the ESA.

Pursuant to nonbinding settlement agreements, the agencies are working together to complete consultations on nine chemicals (diazinon, chlorpyrifos, malathion, methomyl, carbaryl, atrazine, simazine, propazine, and glyphosate) by December 2022.

II. STATUS UPDATE

EPA released the draft biological evaluations (BE) for chlorpyrifos, diazinon, and malathion for public comment, April 2016, and released final BEs January 2017. The BEs analyzed the effect based on the authorized label use. Based on manufacturer and sales data we know the labels overestimate actual pesticide use.

The Service prepared preliminary draft biological opinions in September 2017 for these three pesticides and requested Solicitor review.

After Solicitor review, the Service determined that a new analyses based upon usage data is necessary to prepare biological opinions consistent with the ESA and its implementing regulations. Because listed species often occur within narrow geographic areas, information on actual use and usage at a more refined spatial scale is necessary to analyze effects *reasonably certain to occur* to such species.

The Service requested additional information regarding actual pesticide usage from EPA and the applicants necessary to complete formal consultation. Alongside this request, the Service sought an extension to the timeframe for the consultation. EPA and the applicants subsequently agreed to extend the consultation for malathion to March 2021.

The Service, EPA, the U.S. Department of Agriculture, and the National Marine Fisheries Service are working together to gather and incorporate refined usage data into the consultation.

In addition, the Service has met with registrants and user groups to gather additional usage data.

While this review and refinement in process has necessitated delaying the completion and release of the draft biological opinions, it will ultimately ensure that the final biological opinions are legally sound and based on the best scientific and commercial data available.

The Service estimates completing consultation and issuing a final biological opinion for malathion in March 2021. We anticipate developing revised timelines for the reviews of diazinon and chlorpyrifos as we learn more from the malathion consultation.

III. POTENTIAL ISSUES

Congress, specifically the House Committees on Natural Resources and Agriculture as well as the Senate Committee on Agriculture, have been interested in the progress made toward completing biological opinions for the nine pesticides and working with stakeholders of the U.S. Department of Agriculture.

The pesticide industry, agriculture community, and environmental non-governmental organizations have also been interested in the ESA compliance of FIFRA. The agencies have conducted five stakeholder workshops to ensure stakeholder engagement in the process.

SEC. 4003. TEMPORARY OPERATIONAL FLEXIBILITY FOR STORM EVENTS.

(a) In General.--

(1) Nothing in this subtitle authorizes additional adverse effects on listed species beyond the range of the effects anticipated to occur to the listed species for the duration of the smelt biological opinion or salmonid biological opinion, using the best scientific and commercial data available.

(2) When consistent with the environmental protection mandate in paragraph (1) while maximizing water supplies for Central Valley Project and State Water Project contractors, the Secretary of the Interior and the Secretary of Commerce, through an operations plan, shall evaluate and may authorize the Central Valley Project and the State Water Project, combined, to operate at levels that result in OMR flows more negative than the most negative reverse flow rate prescribed by the applicable biological opinion (based on United States Geological Survey gauges on Old and Middle Rivers) daily average as described in subsections (b) and (c) to capture peak flows during storm-related events.

(b) Factors to Be Considered.--In determining additional adverse effects on any listed fish species beyond the range of effects anticipated to occur to the listed fish species for the duration of the smelt biological opinion or salmonid biological opinion, using the best scientific and commercial data available, the Secretaries of the Interior and Commerce may consider factors including:

(1) The degree to which the Delta outflow index indicates a higher level of flow available for diversion.

(2) Relevant physical parameters including projected inflows, turbidity, salinities, and tidal cycles.

(3) The real-time distribution of listed species.

(c) Other Environmental Protections.--

(1) State law.--The actions of the Secretary of the Interior and the Secretary of Commerce under this section shall be consistent with applicable regulatory requirements under State law.

(2) First sediment flush.--During the first flush of sediment out of the Delta in each water year, and provided that such determination is based upon objective evidence, the Secretary of the Interior shall manage OMR flow pursuant to the portion of the smelt biological opinion that protects adult Delta smelt from the first flush if required to do so by the smelt biological opinion.

(3) Applicability of opinion.--This section shall not affect the application of the salmonid biological opinion from April 1 to May 31, unless the Secretary of Commerce finds that some or all of such applicable requirements may be adjusted during this time period to provide emergency water supply relief without resulting in additional adverse effects on listed salmonid species beyond the range of the effects anticipated to occur to the listed salmonid species for the duration of the salmonid biological opinion using the best scientific and commercial data available. In addition to any other actions to benefit water supply, the Secretary of the Interior and the Secretary of Commerce shall consider allowing through-Delta water transfers to occur during this period if they can be accomplished consistent with section 3405(a)(1)(H) of the Central Valley Project Improvement Act and other applicable law. Water

transfers solely or exclusively through the State Water Project are not required to be consistent with subsection (a)(1)(H) of the Central Valley Project Improvement Act.

(4) Monitoring.--During operations under this section, the Commissioner of Reclamation, in coordination with the Fish and Wildlife Service, National Marine Fisheries Service, and California Department of Fish and Wildlife, shall undertake expanded monitoring programs and other data gathering to improve the efficiency of operations for listed species protections and Central Valley Project and State Water Project water supply to ensure incidental take levels are not exceeded, and to identify potential negative impacts, if any.

(d) Effect of High Outflows.--When exercising their authorities to capture peak flows pursuant to subsection (c), the Secretary of the Interior and the Secretary of Commerce shall not count such days toward the 5-day and 14-day running averages of tidally filtered daily Old and Middle River flow requirements under the smelt biological opinion and salmonid biological opinion, unless doing so is required to avoid additional adverse effects on listed fish species beyond those anticipated to occur through implementation of the smelt biological opinion and salmonid biological opinion using the best scientific and commercial data available.

(e) Level of Detail Required for Analysis.--In articulating the determinations required under this section, the Secretary of the Interior and the Secretary of Commerce shall fully satisfy the requirements herein but shall not be expected to provide a greater level of supporting detail for the analysis than feasible to provide within the short timeframe permitted for timely real-time decisionmaking in response to changing conditions in the Delta.

APPENDIX

Description of the Proposed Action

The proposed Federal action addressed in this Opinion (hereafter, the Action) is the registration of chlorpyrifos under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). The FWS considers the duration of the Action to be 15 years, accounting for the 15-year registration cycle for FIFRA Section 3 and Section 24(c) registration, and the applicable duration for other uses for this chemical, unless otherwise specified on the product labels. The following chemical-specific descriptions are taken largely from EPA's BE for chlorpyrifos.

For this pesticide, the Action includes registration of the uses, as described by product labels, of all pesticide products containing the active ingredient, its metabolites and degradates, any other active ingredients, other ingredients within the formulations (e.g., adjuvants and inert ingredients), and any recommended tank mixtures. The Action also includes all authorizations for use of pesticide products, including the use of existing stocks, and active labels of products containing the active ingredient. A complete listing of product uses is found in the Agricultural and Non-agricultural Uses sections below.

In their BE, EPA considered the likely use types of the products over the duration of the Action, although the Agencies recognize future uses are difficult to predict with either accuracy or precision, particularly as more time passes. Thus, future uses have been addressed to the extent possible in EPA's BE where the geographic distribution and magnitude of exposure (including application rate and methods of application) have been included in the scope of the assessment. Where new uses, rate increases, or an application method that increases exposure beyond what was addressed in the BE and this Opinion are approved or proposed, re-initiation of consultation would be required.

The purpose of the Action, as noted in EPA's BE, is to provide tools for pest control on food and feed crops, as well as other non-agricultural uses that do not cause unreasonable adverse effects to the environment throughout the United States and its affiliated territories. For additional information on the registration and re-registration review processes, see section 1.1.1. of the Problem Formulation in the BE. The following sections describe the Action in greater detail, and are taken largely from EPA's BE for chlorpyrifos.

Rate, Frequency, and Number of Applications

Estimated environmental concentrations are influenced, in part, by the allowable manner of pesticide use as described by the label, including the application rate, frequency of application, and the maximum number of applications per season or year. For each use category, EPA modeled EECs in a number of ways. (b) (5) - DPP

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Determining Percent of the Population That Could Be Exposed to Chlorpyrifos

Overlap with species range: The estimate of exposure for each species is derived, in part, by determining the extent that the range of a species overlaps with use site categories for which the pesticide is registered, combined with anticipated off-site transport. The process for establishing the use site footprint is described in Attachment 1-3 of EPA's BE. Briefly, chlorpyrifos use sites were binned (i.e., categorized) by the general land cover class that best represents the use pattern (e.g., grapes are categorized with orchards and vineyards while cole crops - e.g., broccoli, Brussels sprouts, cabbage, cauliflower, collards, kale, and kohlrabi - are binned with other vegetables). Information on crop or use, application timing, application rates, method and any geographic restriction is contained in the Master Use Summary Table (Appendix 1-3 of the BE, Master Use Summary Table for Chlorpyrifos). To map use sites on the landscape, EPA used the 2014 National Agricultural Statistics Service (NASS) Census of Agriculture (CoA) crop acreage reports and the 2012 NASS CoA crop harvested data to confirm the presence or absence of individual use sites or crop within a Hydrologic Unit Code (HUC) 2 region. Unless the label limits a use pattern to a particular geographic area, all regions are modeled where there are crop acres or harvested data. For those crops/use sites where NASS harvested data are unavailable, the crop or use site was assumed to occur within that HUC2 region. Limited data are available for crops grown in the Pacific Islands and Caribbean.

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Pesticide usage: (b) (5) - DPP [Redacted text]

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For the analysis of effects to species, we assume that (b) (5) - DPP

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Consultation Process

Interagency Consultation

- Discretionary agency action, here the approval or registration:
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 - Look at: Effects of agency action to the environmental baseline and determine if jeopardizes continued existence or adversely modifies or destroys designated critical habitat
- Effects of the Action: Direct Effects (Immediate effects of the action - (b) (5) - DPP), Indirect effects (effects to species that are "caused by the action," are "later in time" and are "reasonably certain to occur" – (b) (5) - DPP)
- commutative effects (private and state actions, within action area – that establish baseline)
- "May effect": Right to formal, or request Not Likely to Adversely Effect if beneficial, insignificant or discountable –must not be capable of measuring) and agency concurs.
- Draw an area look at everything in area without action and without
- (b) (5) - DPP .

Where We Are At

- Longstanding difficulty completing pesticide consultations

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Options Going Forward

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Policy Direction

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- Because of the widespread use of chlorpyrifos and the uncertainty with where the mosquito adulticide, wide area, and non-agricultural uses could occur, the entire United States is considered the action area for chlorpyrifos for Step 1. For Step 2, again due to the uncertainty with where the adulticide, wide area, and non-agricultural uses could occur, any of these uses could potentially occur in any watershed, resulting in pesticide contribution to a receiving stream, negating the need to assess downstream dilution for Step 2. A process is being developed to evaluate EECs in upstream reaches, as well as for the streams in the species ranges and critical habitat, for Step 3 in order to address the contribution of the upstream sources to the existing EECs.
- To help determine the potential for risk, effects thresholds are established (see Interim agreement]). For mortality to animals, the one-in-a-million chance of mortality [based either on the 5th percentile of the Species Sensitivity Distribution (SSD) or a surrogate LD₅₀, LC₅₀, or EC_x] is used to assess direct effects to a listed species (for details, see **ATTACHMENT 1-4**). For potential indirect effects based on prey lethality for those species without obligate relationships, the exposure that results in a 10% effect for the 5th percentile species on an SSD for the prey species or the 10% effect level for the most sensitive prey species tested (if not enough data are available for a SSD) is used. For sublethal effects, the direct effects threshold for animals and plants is the lowest available NOAEC/NOAEL or other scientifically defensible effect threshold (EC_x) that can be linked to survival or reproduction. For animals, the indirect effects threshold is the LOAEC/LOAEL for growth or reproduction for relevant taxa. For plants and indirect effects, the threshold is the lowest available LOAEC or EC₅₀ value (aquatic plants) and the lowest LOAEC or EC₂₅ value (terrestrial and wetland plants). These thresholds are used with other available data in a weight-of-evidence (WoE) approach which integrates the body of evidence that is available for making an effects determination. For the exposure assessment, the overlap of species range and action area, the relevance of predictive models to simulate EECs, the quality of fate data for exposure modeling and monitoring data that may be available are considered. For the effects analysis, the number of studies and/or species tested in the available toxicity data, taxonomic surrogacy, the magnitude and/or types of effects observed, and incident data are considered. An overall risk finding (high, medium, low) and a finding on the overall confidence (high, medium, low) in the available exposure and effects data is made for each line of evidence to inform the effect determinations for listed species and critical habitats (see **ATTACHMENT 1-9**).
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- Interim approaches and agreement: <https://www.epa.gov/endangered-species/interim-approaches-pesticide-endangered-species-act-assessments-based-nas-report>

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DRAFT

Rick Keigwin, Director, Office of Pesticide Programs
(Or Marietta Echeverria, Director, Environmental Fate and Effects Division – mailcode 7507P)
U.S. Environmental Protection Agency
Office of Pesticide Programs
Division Mail Code 7501P
1200 Pennsylvania Ave. NW
Washington, D.C. 20460

Subject: Endangered Species Act section 7 consultations on the reregistration of chlorpyrifos, malathion, and diazinon under the Federal Insecticide, Fungicide, and Rodenticide Act

November __, 2017

Dear Mr. Keigwin,

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(b) (5) - DPP, ACP



(b) (5) - DPP, ACP

If you have any questions or concerns about this consultation or the consultation process in general, please feel free to call me at 202-208-4646 or Deputy Assistant Director Gina Shultz at 703-358-1985.

Sincerely,

Description of the Proposed Action

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Pesticide usage: (b) (5) - DPP

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U.S. FISH AND WILDLIFE SERVICE
ASSISTANT DIRECTOR, ENDANGERED SPECIES

1 December 2017

David,

Per your request, we've assembled a catalog of correspondence and documents that reflect agreements between FWS and EPA on how the current consultation of the re-registration review of malathion, chlorpyrifos, and diazinon will be conducted.

Also enclosed are the two FWS documents referenced in the National Academies report. X

Please advise if you have any questions or need additional information.

Cam

1849 C Street NW, Room 3242, Washington, DC 20240, 202/208-4646

Relevant Correspondence/Communications Involving FWS and EPA

Tab A – Enhancing Stakeholder Input in the Pesticide Registration Review and ESA Consultation Processes and Development of Economically and Technologically Feasible Reasonable and Prudent Alternatives: Docket ID EPA-HQ-OPP-2012-0442. March 19, 2013

Describes the section 7 process utilized during pesticide consultations with FWS and NMFS and specifically refers to the general regulations at 50 CFR 402 (starting on page 9):

- Services' ESA Consultation Process
Under the Services' ESA regulations¹¹, when a Federal agency determines that its proposed action may adversely affect a listed species or critical habitat, the agency is obligated to enter into formal consultation with the Services to ensure that the action is not likely to result in jeopardy to the listed Species, or destroy and/or adversely modify critical habitat.
 - ¹¹ See 50 CFR part 402

Establishes registrants as applicants under the ESA (page 9):

- When EPA determines that formal consultation with one or both of the Services is necessary, continued engagement with registrants and interested stakeholders (e.g., growers, state agencies, conservation groups, and water quality groups) is vital. Under ESA regulations, registrants are considered "applicants." Applicants have certain defined opportunities under the regulations, including the opportunity to submit information during the consultation and review draft biological opinions.

Tab B – Interim Approaches for National-Level Pesticide Endangered Species Act Assessments Based on the Recommendations of the National Academy of Sciences Report (November 15, 2013)

Outlines interim approaches, (b) (5) Generated for a public outreach meeting with EPA, NMFS, FWS, USDA, registrant representatives, and non-governmental organizations. This meeting was held to talk about interim approaches, both short- and long-term, for the Agencies to implement, based on what was recommended from the NAS report.

Tab C – Interim Report to Congress on Endangered Species Act Implementation in Pesticide Evaluation Programs; November 2014 - does not mention counterpart regs.

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Tab D – Consultation Initiation Letter for Chlorpyrifos, Diazinon and Malathion; January 18, 2017

Letter states that EPA is requesting consultation under 50 CFR Part 402.46, Optional Formal Consultation Procedures for FIFRA Actions

Tab E – Request from FWS to EPA for additional information (November 14, 2017)

Cites to the default interagency consultation regulations at 50 CFR Part 402.14 as the basis for the request.

Tab F – Response from EPA to request for additional information (November 17, 2017)

Affirms that the request for additional information is based on the default interagency regulations and not the EPA/FIFRA counterparts.

Correspondence between FWS and NAS, as referenced in NAS report

Tab G – Informal Consultation on the Effects of Diazinon and Racemic Metolachlor Reregistration on the Endangered Barton Springs Salamander. Letter to Arthur-Jean B. Williams, Environmental Fate and Effects Division, Office of Pesticide Programs, U.S. Environmental Protection Agency, from M.A. Nelson, Division of Consultation, Habitat Conservation Planning, Recovery and State Grants, U.S. Fish and Wildlife Service, Washington, DC. January 14, 2009.

Non-concurrence letter on EPA's on two NLAA determination by EPA for the Barton Springs salamander.

Tab H – Response to NAS Committee Questions, from Rick Sayers, Chief, Division of Consultation, HCPs, Recovery, and State Grants, U.S. Fish and Wildlife Service Endangered Species Program. March 28, 2012.

FWS responses to 26 specific questions posed to the agencies by the NAS panel covering topics from each of the charge questions.

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ENVIRONMENTAL PROTECTION AGENCY
Office of Chemical Safety and Pollution Prevention
Office of Pesticide Programs

**Enhancing Stakeholder Input in the Pesticide Registration Review and ESA Consultation
Processes and Development of Economically and Technologically Feasible Reasonable and
Prudent Alternatives**

Purpose of this Document:

This document, which was developed jointly by the EPA, the U.S. Department of Agriculture (USDA), the National Marine Fisheries Service (NMFS) in the U.S. Department of Commerce and the Fish and Wildlife Service (USFWS) in the U.S. Department of Interior¹, provides guidance to staff and managers participating in the associated processes. It does not create or confer legal rights or impose any legally binding requirements on the agencies or any other party.

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¹ NMFS and USFWS are referred to collectively as the Services.

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1 Introduction

This document pertains to Federal agency implementation of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)² and the Endangered Species Act (ESA)³. This document describes how the agencies will implement the statutes in the context of pesticide registration review decisions. In August 2012, EPA published a draft proposal and solicited public comments for 60 days. EPA, USDA, and the Services subsequently revised the document after consideration of the public comments received.

The process of assessing the potential effects of a pesticide to federally listed threatened and endangered species (hereafter referred to as listed species), determining whether risk reduction measures are necessary to ensure these species are not likely to be jeopardized and critical habitat is not destroyed or adversely modified, and implementing such measures requires close coordination across multiple Federal agencies and impacts a variety of entities including state pesticide regulatory agencies, pesticide users and pesticide companies. The process of ensuring protection of these species is one that will benefit from input by these entities as well as the general public. There are multiple opportunities for soliciting and considering such input at various points in the process as noted below. Because stakeholders, including state governments, universities, and growers/users have significant amounts of relevant information and are the ultimate implementers of pesticide labels in the field, it is critical that they have a seat at the table during the development of any needed risk reduction measures to ensure that such measures are technologically and economically feasible.

Over the past several years, stakeholder groups have increasingly expressed interest in ESA issues involving pesticide registration. Furthermore, Congressional committees have also stressed the importance of an open and transparent process ensuring that at multiple stages of the process there are opportunities for broader public participation and that the economic impacts on agriculture are more fully integrated into the process before a final decision is made. This paper describes how the Federal agencies can clarify and/or modify their processes to address these concerns and increase the robustness of the overall process. This paper specifically describes changes to EPA's registration review process and the Services' Section 7 consultation process that are intended to facilitate ESA pesticide consultations and coordination across these Federal agencies. In addition, it calls for a greater role for USDA.

These process changes recognize and acknowledge the respective expertise of the four agencies involved. USDA's expertise on crop distribution and their relationships with the agricultural community are critical links between EPA's expertise on pesticides and the Services' expertise on listed species' locations, status, and biology. Each agency's expertise defines their respective roles and responsibilities during consultation.

2 EPA's Registration Review Program

The Food Quality Protection Act (FQPA) of 1996 amended FIFRA to include a mandate that EPA establish a new program⁴, called registration review⁵, so that, as the ability to assess risk evolves

² 7 U.S.C. 136a *et seq.* (<http://www.epa.gov/lawsregs/laws/fifra.html>).

³ 16 U.S.C. §1531 *et seq.* (<http://www.epa.gov/lawsregs/laws/esa.html>).

⁴ FIFRA Section 3(g), 7 U.S.C. 136a(g).

⁵ For more information about EPA's registration review program, go to http://www.epa.gov/oppstrd1/registration_review/.

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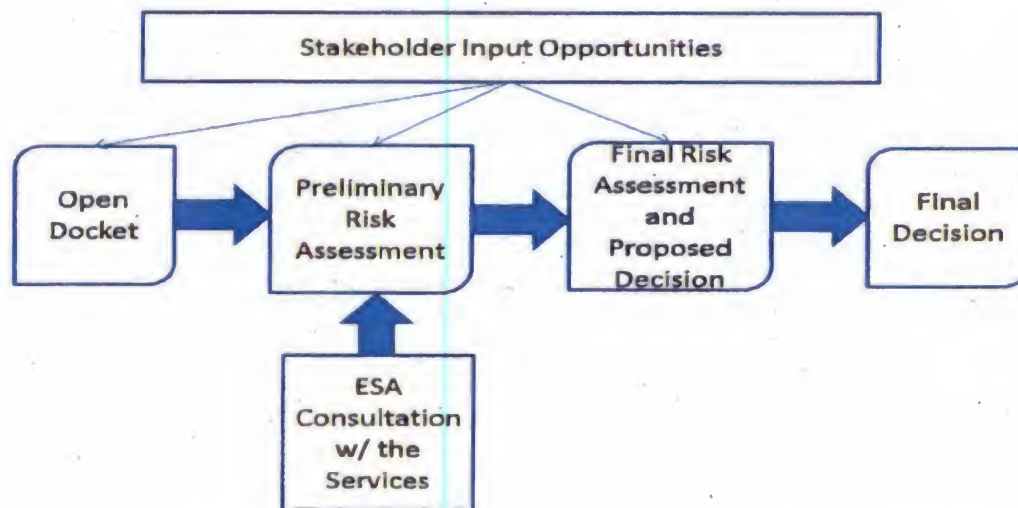
and as policies and practices change, all registered pesticides continue to meet the statutory standard of no unreasonable adverse effects to human health and the environment. Changes in science, public policy, and pesticide use practices will occur over time. Through the registration review program, EPA periodically reevaluates pesticides to ensure that as change occurs, products in the marketplace can still be used safely. The registration review program challenges EPA to continuously improve its processes, science, and information management while maintaining a collaborative and open process for decision-making. In general, EPA intends to accomplish its work relative to protection of listed species in the course of its registration review program. That work will include, where appropriate, consultation with the Services.

Under EPA's regulations, the registration review program is a multi-stage process, incorporating opportunities for public comment at critical points in the review process. As originally designed, interested stakeholders can comment on and provide relevant information at three critical points during the registration review process: the initial docket opening, the preliminary risk assessment, and the proposed decision. These points in the process are publically announced and accompanied by time frames and deadlines for the submission of comments and relevant information.

At the stage where EPA opens the registration review docket, the Agency issues a preliminary work plan and invites the public to provide feedback on how EPA will scope the review (i.e., problem formulation) and what data will be required as part of this review. Following the completion of the public comment period, EPA reviews the information submitted, develops a response to comments document, and issues a final work plan. After the required data have been submitted and evaluated, EPA develops a preliminary risk assessment that addresses potential human health and ecological exposures and issues that scientific analysis for public comment.⁶ EPA's ecological risk assessments will become a "biological evaluation" during consultation with the Services. After reviewing public comments, EPA revises the risk assessment, as needed, develops a response to comments document, proposes risk reduction measures it believes are necessary to address risk concerns, and invites the public to provide feedback on its proposed decision. It is only after these multiple stages of public comment that the Agency issues its final registration review decision. Figure 1 provides an overview of the original registration review program.

⁶ When originally designing the registration review program, EPA intended to initiate consultation with the Services (if needed) at the point in the registration review process where comments were being sought on the preliminary risk assessment. The concept was that while the Agency was soliciting public input on the preliminary assessment, EPA would also engage in consultation with the Services, resulting in a Biological Opinion that could be incorporated into a final risk assessment and proposed registration review decision at the next step in the process.

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Figure 1. Original Design of EPA's Registration Review Program

Over the past year, EPA has engaged in significant dialogue with the Services and other stakeholders regarding how to improve the registration review process. At a summary level, most stakeholder groups have recommended that EPA make changes to its process to accomplish several goals: 1) earlier stakeholder involvement in the scoping of the pesticide's re-evaluation, 2) earlier adoption of risk reduction measures, including incorporation of clarifications and/or new restrictions on product labels, before initiation of any needed consultations with the Services and prior to completion of the registration review, and 3) a more focused consultation process (when and if necessary) that reflects the adoption of such measures.

3 Process Improvement Discussions

In May 2011, the Minor Crop Farmer Alliance (MCFA) convened a workshop in Denver, Colorado, with three primary goals:

- Provide grower representatives with an understanding of the processes and analyses leading to the identification of risk and risk reduction options by EPA and by the Services.
- Identify grower-level data that could potentially refine the risk assessment and enhance the risk identification and risk reduction decision processes.
- Initiate discussions on the mechanisms for providing such data.

Several questions emerged from these discussions and have served to inform potential improvements to the registration review and consultation processes:

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- What are the appropriate points in the registration review process to initiate discussions with both the registrant and the user community to identify, describe and verify crop specific use and usage information?
- What data sources are most complete and relevant to the risk assessment process?
- How will commodity groups know when to engage in the process?
- How will the agencies ensure that information collected and submitted is considered?

Subsequent to the workshop, EPA solicited input from its Federal advisory committee, the Pesticide Program Dialogue Committee (PPDC), regarding potential process changes that would facilitate greater opportunities for public participation and transparency in the registration review process and have the additional benefit of streamlining ESA consultation with the Services.

After considering public feedback based on the August 2012 proposal, and advice from the PPDC, EPA has implemented changes to the registration review process further augmenting opportunities for public involvement in the process. These changes are described below.

Earlier involvement of stakeholders in the Registration Review Process

As part of the registration review process, EPA annually publishes a four-year schedule to communicate when individual pesticides will enter the registration review program. To enhance transparency in the process, EPA has begun including information on the specific timeframe within any fiscal year when a pesticide will begin its review. Having this information available in advance provides early notice for interested stakeholders to submit information to EPA in advance of the pesticide beginning its re-evaluation⁷.

During FY12, EPA began holding "Focus" meetings during the early stage of registration review. EPA believes that these meetings increase efficiency and help to better inform the problem formulation and risk assessment phases of the registration review process. EPA uses "Focus" meetings to begin initial outreach efforts to stakeholders. A "Focus" meeting is initiated by EPA with affected registrants and possibly other stakeholders via invitation⁸. EPA will extend invitations to USDA, and, where applicable, to the Services, to attend "Focus" meetings. The USDA can help identify affected growers and ensure they are aware of time frames for registration review. The Services can respond to questions and concerns regarding any existing ESA issues, such as, ongoing litigation.

In an effort to create a transparent process and broaden stake holder participation, EPA will place the "Focus" meeting minutes and related materials (the invitation letter, a sign-in sheet containing contact information for the meeting attendees, documents provided by the EPA, registrants, or other attendees, and any other related material) in the publically-available,

⁷ For more on registration review schedules go to http://www.epa.gov/oppsrrd1/registration_review/schedule.htm

⁸ For more details on "Focus" meetings visit: http://www.epa.gov/oppsrrd1/registration_review/focus-meetings.html

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chemical-specific registration review dockets within 45 days⁹, but will strive to have those materials posted to the docket within 10 business days of the meeting. Additional follow-up meetings and calls will be held as needed. If upon reviewing the minutes and materials of the meeting, an interested stakeholder wishes to meet with EPA and discuss these issues, they can contact EPA and request a meeting. Contact information for EPA will be included in the chemical-specific docket materials. EPA can initiate discussions with registrants and other parties at any point in the registration review process.

Similar to the "SMART" meetings that were held during reregistration, these "Focus" meetings provide the registrants and other interested stakeholders opportunities to: 1) identify the uses that the registrant intends to support for registration review, 2) address label language that is vague, insufficient, or inaccurate at an early stage of the review process, and 3) adopt risk reduction measures before registration review begins.

Purpose #1: Define the use patterns supported by the registrants. Markets and the economic viability of certain pesticide uses change over time. Through the "Focus" meetings, EPA will ask the manufacturers to explicitly indicate which uses they intend to continue to support for registration. This provides an opportunity to begin the process of defining the scope of the Federal action to be considered under the ESA.

Purpose #2: Ensure label language accurately reflects product use and usage. Inaccuracies, missing information, and vague or poorly worded label language should be identified. Confusion regarding label directions will be addressed at this stage in the process so that the risk assessment more accurately reflects the intended use of the pesticide. One such example is inclusion of specificity on the maximum number and frequency of applications. Products and use patterns can be discussed to maximize the potential for species' protections while maintaining a critical use. When applicable, EPA will follow-up with additional meetings with state regulators, USDA, and commodity groups on proposed use site/label changes.

Purpose #3: Identify potential risk drivers and potential risk reduction measures as early as possible. Previous risk assessments, conducted either to support reregistration decisions, new uses, or litigation, may have indicated potential ecological risks. Alternative chemicals may have been developed since those initial evaluations; as a result, the benefits of the pesticide beginning registration review may have changed. There may also be the potential, based upon further field experience with the pesticide, to identify the key efficacious rates critical for crop protection and/or existing conservation practices being employed that could be incorporated into labels as part of "early risk reduction."

It is a common goal of the Federal agencies to have accurate use and usage language on product labels, and, when possible, agreed upon risk reduction measures incorporated onto product labels before the pesticide reaches the preliminary risk assessment stage. This saves valuable resources for all.

⁹ Under the registration review rule (40 CFR 155.52), the EPA has 45 days to docket meeting minutes and related materials. A special Focus Meetings docket has been established for meeting material; visit EPA-HQ-OPP-2012-0778 at www.regulations.gov.

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Consideration of pesticide use and usage data

During a two to three-year period of time after completion of the final workplan, the registrant is often developing toxicity and exposure data to support the preliminary risk assessment for the pesticide's registration review. As this information is being submitted to EPA, updated use data (i.e., data identifying registered use sites) and usage information (i.e., information explaining how products are applied to specific use sites) will be solicited from a variety of sources, including USDA and grower organizations. These data, such as application methods, application rates, frequency of application, and application timing are critical pieces of information in developing EPA's ecological risk assessment. For example, having more complete information on the times of the year when a pesticide is used may enable EPA to more accurately predict the potential exposure of listed species to pesticides.

EPA will incorporate these data, which may be national and/or local in scope, to refine the label and/or identify typical use rates for risk characterization, to define the uses that will be supported for registration review, and to facilitate the potential adoption of any additional needed risk reduction measures with the possibility of reducing, or eliminating the number of "may affect, likely to adversely affect" determinations under the ESA. These data can also be used to describe the situations in which rates higher than "typical" rates are needed and under what conditions, allowing more prescriptive label language to be developed. Ultimately, these data should result in a refined preliminary (ecological) risk assessment.

EPA has a long history of using these data in making pesticide safety determinations. For example, pesticide usage data collected by USDA's National Agricultural Statistics Service (NASS) have been found to be of exceptional quality and reliability in making food safety determinations (i.e., "reasonable certainty of no harm" determinations) under the FQPA. Congress has directed EPA to use data, such as those developed by NASS when EPA "finds that the data are reliable and provide a valid basis to show what percentage of the food derived from such crop is likely to contain such pesticide chemical residue," provided that the Agency periodically reevaluates the estimate of the anticipated exposure in light of these data.

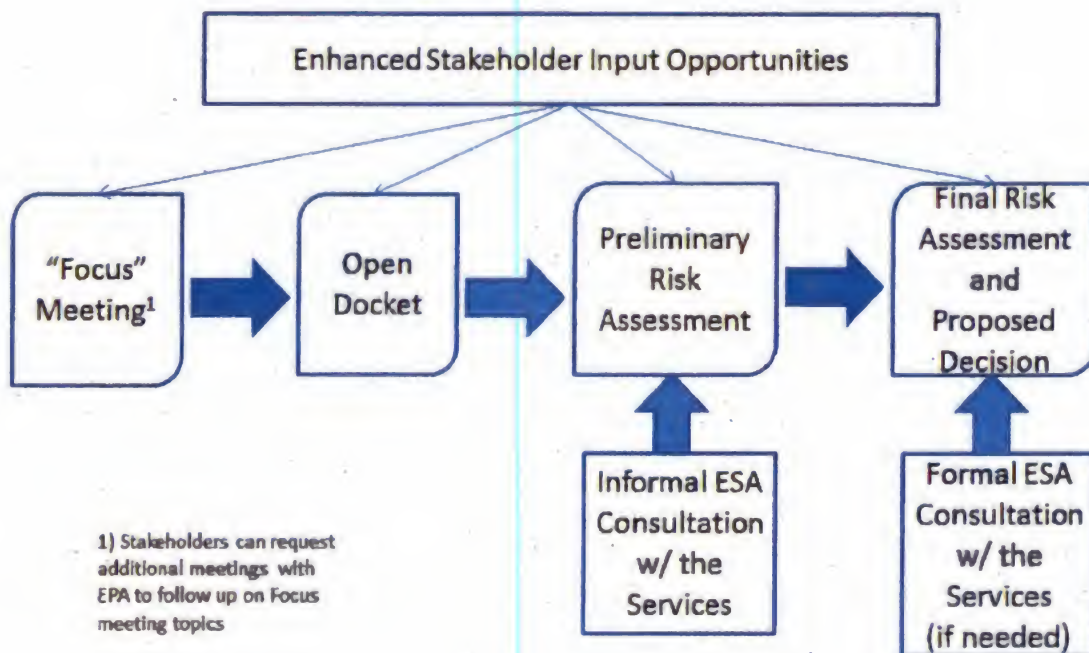
Increased use of the informal (or early) consultation process

A critical step in developing the preliminary ecological risk assessment is having reliable data on species habitat, diet, geographic range, and behavior. EPA will use the informal consultation process to work with the appropriate Service to gather this information for inclusion in a more refined ecological risk assessment. Collaborating with the Services to gather this information at an earlier stage in the process has a number of benefits, including 1) incorporation of more refined species biology and habitat information into EPA's effects determinations, 2) potential reduction in the number of "may affect, likely to adversely affect" determinations, and 3) fewer resources (for both EPA and the Services) needed to complete consultations because the best available information has been incorporated into EPA's preliminary ecological risk assessment. Early interaction under informal consultation will allow EPA and the Services to identify potential risk to listed species and their habitats and would position EPA to begin discussing potential risk reduction measures with the pesticide registrant. Even when this informal consultation does not eliminate the need for formal consultation, the work accomplished through informal consultation will inform and streamline the formal consultation.

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As a result of the process improvement discussions, EPA is making two significant changes to its registration review process: 1) hold "Focus" meetings at the start of the registration review for each active ingredient, and 2) consult informally with the Services early in the review process and initiate any needed formal consultations at a subsequent stage. Figure 2 outlines EPA's revised registration review process.

Figure 2. Revised Design for EPA's Registration Review Process



One major end result of these process changes is that through public involvement, particularly with growers who are responsible for "on the ground" implementation of pesticide product label language, risk reduction measures that achieve protection for listed species and designated critical habitat and that are technologically and economically feasible can be achieved, possibly through changes to labels, or via species' bulletins¹⁰. The involvement of growers and state lead agencies will also ensure that the protection measures are economically and technologically feasible.

¹⁰ More on EPA's Bulletins Live! can be found at <http://www.epa.gov/oppfead1/endanger/bulletins.htm>

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4 Services' ESA Consultation Process

Under the Services' ESA regulations¹¹, when a Federal agency determines that its proposed action may adversely affect a listed species or critical habitat, the agency is obligated to enter into formal consultation with the Services to ensure that the action is not likely to result in jeopardy to the listed species, or destroy and/or adversely modify critical habitat.

However, before initiating formal consultation under section 7 of the ESA, a Federal agency, or a designated non-Federal representative can consult "informally."¹² Informal consultation is an optional process that can be used to (1) clarify whether and what listed, proposed and candidate species, or designated, or proposed critical habitat may be in the action area; (2) determine what effect the action may have on these species and critical habitat; (3) explore ways to modify the action to reduce or remove adverse effects to the species and critical habitat; (4) determine the need to enter into formal consultation; and (5) explore modifications of an action to benefit listed species. Participants in informal consultation may include the (1) Federal action agency, (2) applicant, (3) non-Federal representative, or (4) consultant working on behalf of one of the first three. There is no overall timetable for informal discussions, and dialogue can continue as long as the parties are willing to participate and are actively working to complete the consultation. If during informal consultation the Federal agency determines, with written concurrence of the Services, that the action is not likely to adversely affect listed species or critical habitat, the consultation process is terminated.

When EPA determines that formal consultation with one or both of the Services is necessary, continued engagement with registrants and interested stakeholders (e.g., growers, state agencies, conservation groups, and water quality groups) is vital. Under ESA regulations, registrants are considered "applicants." Applicants have certain defined opportunities under the regulations, including the opportunity to submit information during the consultation and review draft biological opinions.

Upon receiving a request to initiate formal consultation from EPA, the Service will convene a meeting with EPA and the applicant to identify what additional information – beyond that provided by EPA in its package initiating consultation – can be provided for consultation and subsequent drafting of the biological opinion. To ensure that all agency expertise is involved, EPA will extend an invitation to USDA to attend the applicant meetings. During consultation, the Services may discuss with EPA its risk assessment and effects determination to gain a better understanding and they may seek out additional information from other sources. If the Services believe that changes to the pesticide label may be necessary to avoid or reduce the extent of adverse effects to listed species or critical habitat, they will work with EPA and USDA to engage the applicant, product users, and other stakeholders to discuss possible label changes needed to avoid jeopardizing the continued existence of listed species and destroying or adversely modifying critical habitat. Before analyzing the effects of the action, the Services, EPA, and applicants will review and agree upon the description of the action (e.g., use rates, registered uses, scope of the proposed action as described on pesticide labels).

The Services will prepare draft biological opinions that include their analyses and conclusions regarding whether use of the pesticide is likely to jeopardize the continued existence of a federally-listed

¹¹ See 50 CFR Part 402.

¹² Endangered Species Consultation Handbook, USFWS and NMFS March 1998; 50 CFR 402.13

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species or to destroy or adversely modify critical habitat under their purview. If FWS and/or NMFS determine that jeopardy or adverse modification of critical habitat is likely, they are obligated to work with EPA and the applicant to identify Reasonable and Prudent Alternatives (RPAs), to the extent such measures exist, to insure that the action will avoid the likelihood of jeopardizing listed species or destroying or adversely modifying critical habitat. Service regulations require that these are measures that can be implemented in a manner consistent with the intended purpose of the action, can be implemented within the scope of EPA's legal authority and jurisdiction, and are economically and technologically feasible. Where the Services anticipate "take"¹³ of listed species, the draft biological opinion(s) includes proposed Reasonable and Prudent Measures (RPMs) and terms and conditions to minimize the impact of the take.

The Services will provide EPA with the draft biological opinion for their review. EPA will make the draft biological opinion available for public comment. The public comment period provides another opportunity for stakeholders to provide valuable input on RPAs, RPMs, and terms and conditions, as well as to provide/suggest/propose alternate risk reduction measures that accomplish the same protection goals but may be easier/less costly for the grower/user community to implement. All comments will be submitted to EPA, although the applicant may send a copy of its comments directly to the Service. EPA will organize the comments and highlight those of particular note and provide them to the Services.

During the public comment period, EPA and the Services, supported by USDA, will solicit input from growers and other stakeholders on any technologically and economically feasible approaches that minimize the impact on growers and that allow them to meet their pest control needs while achieving the necessary protection goals to avoid jeopardy to threatened and/or endangered species. In particular, this process should offer stakeholders an opportunity to provide data and to identify practical considerations that affect the viability of different options for mitigating risks to species. EPA will provide a key role by focusing affected entities on the availability of the draft biological opinion and timeframes for submission of input.

Upon receipt of the organized public comments from EPA, each Service will prepare a document for their respective opinions, where applicable, and include it in the administrative record that addresses how comments were considered and, if appropriate, how the final document was modified to address the comments. Each Service will include this document in their respective administrative records and will provide it to EPA. Both the Services and EPA will make the document available to the public upon request.

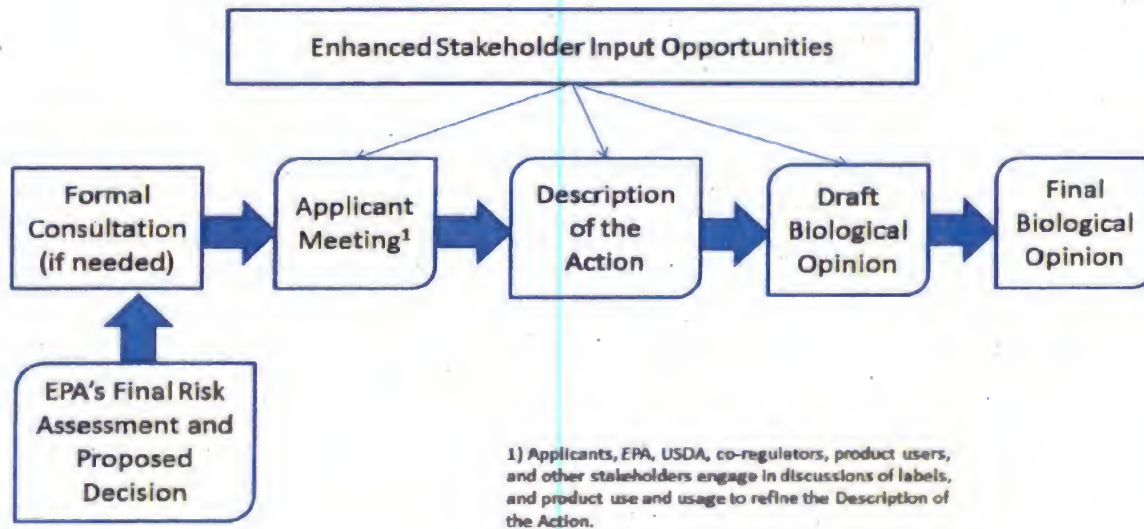
The ESA and section 7 regulations require that formal consultation be concluded within 90 calendar days of initiation, and that the biological opinion be delivered to the action agency within 45 days of the conclusion of formal consultation, unless an extension is agreed to by the agencies and any applicant. EPA will seek an extension to the consultation process when they determine that the statutory timeframes fail to provide adequate time for consideration of information obtained through this process. However, if the extension exceeds more than 60 days, i.e., 150 days from initiation of formal consultation, EPA and the Services must seek consent from the applicants. It should be recognized, however, that circumstances beyond the government's control (e.g., the refusal of an applicant to agree to an extension) may force the process described above to be more truncated.

¹³ Take – to pursue, hunt, shoot, wound, kill, trap, capture, or collect, or attempt to pursue, hunt, wound, kill, trap, capture, or collect. See 50 CFR§10.12.

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Throughout the consultation, it is critical that the established expertise of each agency is recognized and respected: the Services are the expert agencies regarding the species; EPA is the expert agency on pesticide risk assessment, regulation, and the enforceability of labels. USDA will lend its expertise on farming/pest management practices and the technological or economic feasibility of adopting potential risk reduction strategies. Therefore, in developing draft RPAs and RPMs, the Services should include only those risk reduction measures that EPA has the authority to impose and should then defer to EPA to implement these measures using its existing statutory authorities. For example, the Services might identify a level of exposure below which jeopardy would not occur. In response, EPA will implement changes to the pesticide registration that will reasonably ensure that the specified level of exposure is not exceeded. Figure 3 outlines the Service's formal consultation process.

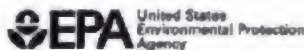
Figure 3. Services' Formal Consultation Process



5 Conclusion

In summary, the Services, EPA, and USDA intend that these changes will result in greater openness and transparency in the pesticide registration review process under FIFRA and in the consultation process under the ESA. Consistent with the statutory mandate to use the best available information, the goal of these changes is to improve stakeholder involvement in these processes and to improve the respective agencies' understanding of how pesticides are used, the ways in which they may affect listed species, and how risks to listed species can be mitigated while preserving the beneficial uses of the pesticides to the extent possible.

We've made some changes to EPA.gov. If the information you are looking for is not here, you may be able to find it on the EPA Web Archive or the January 19, 2017 Web Snapshot.



Interim Approaches for Pesticide Endangered Species Act Assessments Based on NAS Report Recommendations

The interim approaches for the pesticide ESA consultation process described in this document are being developed and will be applied collaboratively as part of EPA's Registration Review program, once they are complete.

You may need Adobe Reader to view files on this page. See EPA's [About PDF](#) page to learn more.

- [Interim Approaches for Pesticide Endangered Species Act Assessments Based on NAS Report Recommendations \(PDF\)](#) (10 pp, 358 K)
- [NAS Report Stakeholder Workshop Presentation \(PDF\)](#) (58 pp, 535 K)

LAST UPDATED ON OCTOBER 6, 2015

Interim Approaches for National-Level Pesticide Endangered Species Act Assessments Based on the Recommendations of the National Academy of Sciences April 2013 Report

I. Introduction

In September 2010, the National Research Council, Division on Earth and Life Studies, Board on Environmental Studies and Toxicology convened the Committee on Ecological Risk Assessment pursuant to the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and the Endangered Species Act (ESA) (Committee). The Committee was convened at the request of the U.S. Environmental Protection Agency (EPA); U.S. Fish and Wildlife Service, and the National Oceanic and Atmospheric Administration's National Marine Fisheries Service (collectively, the Services); and the U. S. Department of Agriculture (referred to as the Agencies). The Agencies jointly requested the examination of scientific and technical issues associated with determining the risk of pesticide registration and use to threatened and endangered species protected by the ESA. The Agencies asked the National Academy of Sciences (NAS) to provide advice on a range of subjects related to risk assessment and the consultation process including best available data, consideration of sub-lethal, indirect and cumulative effects, assessing the effects of chemical mixtures and inert ingredients, the role and use of models, uncertainty, and the use of geospatial information and datasets.

On April 30, 2013, the Committee provided their recommendations to the Agencies in the form of a report entitled, *Assessing Risks to Endangered and Threatened Species from Pesticides* (National Research Council, 2013; http://www.nap.edu/catalog.php?record_id=18344). Since then, the Agencies have been working together to develop shared scientific approaches that reflect the advice provided by NAS, and have developed joint interim scientific approaches for assessing the risks of pesticides to endangered and threatened species (hereafter referred to as listed species), based on the NAS recommendations. The Agencies are also working on increasing the opportunities for stakeholder input during the review of pesticide registrations under FIFRA and associated consultations under the ESA.

The interim approaches for the pesticide ESA consultation process, which are based on shared assumptions, data, analytical processes and models, will be applied collaboratively as part of EPA's Registration Review program beginning in 2014. The Registration Review program, mandated under the Food Quality Protection Act (FQPA), makes sure that, as the ability to assess risk evolves and as policies and practices change, all registered pesticides continue to meet the FIFRA statutory standard of no unreasonable adverse effects to human health or the environment. The Agencies will work together to develop refined and improved techniques and approaches over time.

Described below in Section II are the general agreements reached by the EPA, FWS, NMFS and USDA. Section III outlines the interim processes that will be used for the initial pesticide consultations conducted under registration review.

II. General Agreements for Pesticide Consultation Process

The Agencies will generally use a three-step consultation process, as outlined in the NAS report (NRC, 2013) [*i.e.*, Step 1 ('No Effect/May Affect' determination), Step 2 ('Not Likely to

Adversely Affect (NLAA)/Likely to Adversely Affect (LAA)' determination), and Step 3 ('Jeopardy/No Jeopardy' determination and "adverse modification/no adverse modification" determination on effects to designated critical habitat(s)), with the understanding that the data and analyses for each step will be used, when possible, for the subsequent steps (see Figure 1). One goal of the interim approach is a streamlined consultation process that relies on best available data, data relevance, risk characterization, and robust quantitative and qualitative analyses.

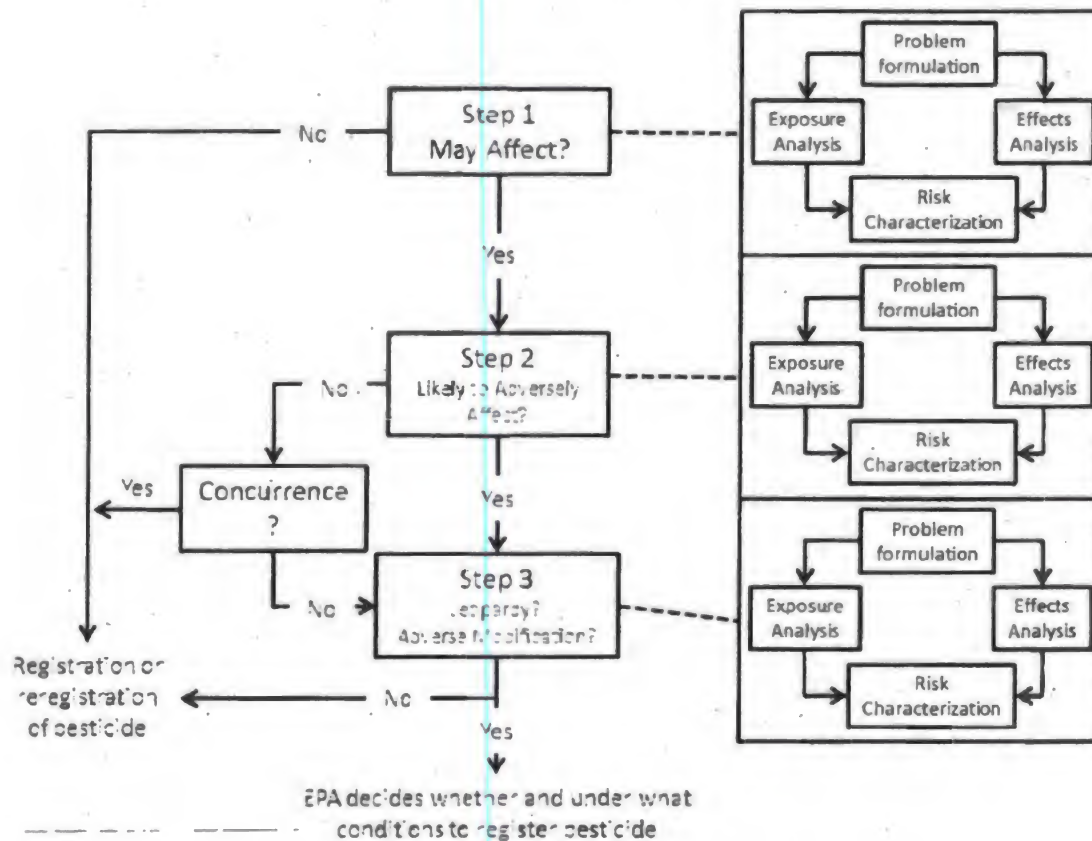


FIGURE 1. Relationship between the ESA process and the ecological risk assessment (ERA) process. Each step answers the question that appears in the box (revised from NRC, 2013, p. 6).

At each step the same four elements – problem formulation, exposure analysis, effects analysis, and risk characterization – should be applied and given the appropriate level of effort needed to address the questions at hand. For example, listed species risk hypotheses are developed during problem formulation for Steps 2 and 3.

The Use of Quantitative and Qualitative Data

In order to address consideration of quantitative and qualitative data as part of the consultation process, the Agencies have agreed to work together to develop criteria for weighing quantitative and qualitative data based on the following guiding principles:

1. Agencies will conduct analyses in a quantitative manner whenever possible.
2. Where information does not meet the criteria for quantitative analyses, the Agencies will utilize the best available science in a qualitative manner, and will be clear as to why qualitative information is being used.
3. The Agencies will jointly develop and apply a systematic approach for using and classifying quantitative and qualitative information.
4. Agency conclusions will be based on a weight-of-evidence approach that includes all the evidence, both qualitative and quantitative, including an explanation of how all of the information was used to draw and support conclusions.
5. As all evidence is being weighed, deference will be given to robust quantitative analyses of relevant data, when available.
6. The Agencies commit to work collaboratively and to share perspectives on judgments being made from the evidence.

"Certainties" and "uncertainties" for quantitative and qualitative approaches will be described. The Agencies will evaluate risk using all of the best available data (quantitative and qualitative) using a weight-of-evidence approach. Where there is no evidence to suggest the existence of a particular effect, the Agencies will not be obligated to produce or create data regarding that effect, although care will be taken to avoid Type 2 errors (*i.e.*, incorrectly concluding no risk) with data-poor species or effects pathways. Risk will not necessarily be assumed in the absence of information nor will the absence of information necessarily be construed as evidence of no risk; rather, professional judgment will be used by considering the significance, quality, and relevance of the available information (including uncertainties) consistent with the Agencies' jointly developed approach for qualitative and quantitative information.

Best Available Data:

In addition to data submitted by pesticide registrants to the EPA as part of the pesticide registration process, the ECOTOXicology database (ECOTOX) (with potential supplementation by the Services) will be used as a source for 'best available' toxicity data. The bibliographies of all of the studies returned by ECOTOX (both those that pass the screening filters and those that do not) will be provided as part of the Biological Evaluation (BE) and all relevant data/information will be used in the effects determination. For example, studies that have not been included in the past because they do not pass the ECOTOX screening filters such as studies having the rejection codes 'Mixture,' 'Incident,' 'Fate,' plus targeted monitoring studies, will be retrieved from the ECOTOX bibliography and considered for use in the weight of evidence analysis. For additional information on ECOTOX and the screening filters see: <http://cfpub.epa.gov/ecotox/>. Additional information, if available, may be provided by the Services to supplement information gathered from ECOTOX.

Exposure models will be used for estimating aquatic environmental concentrations. Targeted monitoring studies may be used for evaluating site-specific exposure estimates. Ambient (general) monitoring results (those studies not coordinated with applications of pesticides at the field scale) will not be used to quantify exposure or to evaluate exposure model performance, but may be used to identify the occurrence of multiple stressors at specific locations for assessing exposure to mixtures. Given the importance of targeted field data to provide an accurate representation of measured aquatic exposures, during the focus meetings with stakeholders, EPA will ask for available targeted field studies and will search the literature (e.g., through ECOTOX) to identify these studies. Information from targeted monitoring studies may be used to inform problem formulation and refine exposure modeling analyses.

Inerts and Mixtures:

For assessments conducted using the interim approach, inerts and mixtures (*i.e.*, formulated products with more than one active ingredient, tank mixes, and environmental mixtures) will largely be considered qualitatively. Quantitative analyses of formulated pesticide products will be conducted by considering spray drift and direct application to water exposure routes. Field dissipation studies will be used, when possible, to determine the potential impact of inerts on the fate of active ingredients. As part of the interim approach, the environmental fate and toxicity of inerts themselves will be addressed to the extent possible through literature searches, European Union data, Quantitative Structure Activity Relationship (QSARs), and submitted formulated product toxicity data [*i.e.*, available toxicity data submitted on formulated products (e.g., the acute rat toxicity data using formulated product) to compare with toxicity data available for the technical grade active ingredient].

Addressing Changes to the Federal Action:

To address future changes to labeled uses that could affect the action area considered in any final Biological Opinion or letter of concurrence, EPA will use its risk assessment process for Section 3, 18 and 24c registration decisions, for chemicals that have already gone through the registration review process, to determine if the risks have changed since completion of consultation such that exposure is higher or the geographical extent of the action area has expanded. EPA will determine whether risk remains the same, is decreased or increased and will re-initiate consultation if risk increases¹ but not if risk is the same or decreased.

III. Interim Approach:

A. Step 1 (No Effect/May Affect Determination and Action Area):

The 'No Effect/May Affect' determination (NAS' Step 1) will largely be based on the overlap of the action area with the species' ranges and designated critical habitats (*i.e.*, any species or critical habitat that overlaps with the action area will be considered a 'May Affect'). The action

¹ Or if other reinitiation triggers are met [e.g., new species listing/critical habitat designation, new toxicity information, label changes that result in new locations for pesticide use, etc.]

area will be based on potential use sites combined with the range of off-site transport to identify the area of potential effects in and around the use sites.

Readily available geospatial data sets will be used to establish agricultural and non-agricultural pesticide use areas. The Agencies will develop a proposal to aggregate data over multiple time periods to more fully account for past, present and reasonable future use area changes. To determine the area of the potential agricultural use sites, sources of information, including but not limited to the following, may be used to determine potential use sites:

- USDA National Agricultural Statistics Service (NASS) Census of Agriculture data (county level)
- The National Land Cover Database (NLCD)
- The Cropland Data Layer (CDL) and/or CDL aggregated by years

For species range and designated critical habitat geospatial information, priority and weight will be given to spatial data provided by the Services. If sub-county spatial data are not available from the Services for particular species and/or designated critical habitats, an interim approach for supplementing listed species locations will be used. Although the interim approach is still being determined, potential sources of species range data include, but are not limited to the FWS' Environmental Conservation Online System (ECOS) [including the Information, Planning, and Conservation System (IPaC), and the Critical Habitat Portal]; the FIFRA Endangered Species Task Force (FESTF) database; and NatureServe.

Estimated environmental concentrations (EECs) will be based largely on modeled estimates. For aquatic concentrations, existing fate and transport models including the Pesticide Root Zone Model and the Exposure Analysis Modeling System (PRZM-EXAMS), the Agricultural Drift Model (AgDRIFT), the Agricultural Dispersal Model (AGDISP), and the Variable Volume Pond Model will be used to evaluate off-site pesticide transport. In addition to the PRZM-EXAMS farm pond, EECs will be derived for different aquatic habitat bins (to be defined) to more accurately reflect the range of exposure that may occur to aquatic species. For terrestrial exposures, the Terrestrial Residue Exposure Model (T-REX), TerrPlant, AgDRIFT and AGDISP will be used. For more information on these models, see: http://www.epa.gov/pesticides/science/models_db.htm.

The action area will be based on the lowest relevant toxicity value for the most sensitive species in the environment that results in the farthest distance from the use site(s) based on the effects thresholds described below. The aquatic portions of the action area will incorporate/characterize downstream transport. All effects/endpoints considered relevant to the 'No Effect' – 'May Affect' determination will be included in Step 1. The effects/endpoints for all species will be listed and arrayed along an exposure concentration gradient. The effects/endpoints that occur at the lowest concentration or at the 5% level of a species sensitivity distribution (SSD) will be used to establish the off-site portion of the action area; these may include, but are not limited to the following (see Table 1):

- For direct effects to animals based on acute lethality endpoints (LC_{50}/LD_{50}):

- For animals with robust data sets, exposure that results in a one in a million chance of mortality based on the 5th percentile (HC₀₅) species from a species sensitivity distribution (SSD).
 - If there are not enough data for a SSD, the exposure that results in a one in a million chance of mortality based on the most sensitive species tested for each taxon will be used.
- For direct effects with sublethal endpoints (only sublethal effects that can be linked to environmental exposures will be considered):
- For plants, endpoints that can be quantitatively or strongly qualitatively linked to effects on growth, the level corresponding to a reproduction/growth no observed adverse effect concentration or level (*i.e.*, NOAEC/NOAEL) for the most sensitive species will be used.
 - For animals, the lowest available NOEC or other scientifically defensible effect threshold (EC_x) will be used.
 - Endpoints generally will be: a) from *in vivo* studies that are conducted with whole organisms and b) linked to environmentally relevant exposures.
 - Decisions on the use of effects levels other than NOEC values (*i.e.*, EC_x) would involve a consideration of the power of the concurrent NOEC from that study and whether there is sufficient information regarding dose response to establish a different threshold with a reasonable degree of confidence.
 - Establishing "may effect" thresholds for given taxa may also, when supported by professional judgment, be based on toxicity studies that are conducted at the sub-organism level (*e.g.*, on organs or cells), provided they can be linked to environmentally relevant exposures that can influence survival, growth, or reproduction.

TABLE 1. Endpoints to be used in Step 1 (the most sensitive of these thresholds will be used in Step 1 to establish the action area) (these are the same thresholds to be used to assess the potential for direct effects in Step 2).

Taxa (of listed species or obligate species)	Mortality	Sublethal Effects
Birds	Concentration (or dose) that would result in a chance of 1 in a million of causing mortality to an individual. This is calculated by using HC ₀₅ of species sensitivity distribution (SSD) of LC ₅₀ or EC ₅₀ values for taxa and representative slope. If SSD cannot be derived, most sensitive LC ₅₀ or EC ₅₀ will be used.	The lowest available NOEC or other scientifically defensible effect threshold (EC _x) will be used. Endpoints generally will be a) from <i>in vivo</i> studies that are conducted with whole organisms and b) linked to environmentally relevant exposures (see text for details)
Mammals		
Reptiles		
Terrestrial-phase amphibians		
Aquatic-phase amphibians		
Fish		
Aquatic invertebrates		
Terrestrial invertebrates	None	<u>Aquatic plants:</u> <i>Non-vascular</i> - Concentration equal to the lowest value among the available NOAEC and
Aquatic plants		
Terrestrial plants		

Wetland plants		<p>EC₀₅ values for non-vascular aquatic plants <i>Vascular</i> - Concentration equal to the lowest value among the available NOAEC and EC₀₅ values for vascular aquatic plants</p> <p><u>Terrestrial and wetland plants:</u> <i>Monocots</i> - Concentration equal to the lowest value among the monocot NOAEC and EC₀₅ values from the available seedling emergence and vegetative vigor studies <i>Dicots</i> - Concentration equal to the lowest of the dicot NOAEC and EC₀₅ values from the available seedling emergence and vegetative vigor studies <i>Non-angiosperm</i> - Concentration equal to the lowest of the NOAEC and EC₀₅ values from the available seedling emergence and vegetative vigor studies</p>
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For species/critical habitats that do not overlap with the action area (as determined by the process described above), the call will be 'No Effect' and no further analyses will be required (*i.e.*, there is no need for Steps 2 and 3). For species and critical habitats that do overlap with the action area, the call will be "May Affect," and the analysis will proceed with Step 2. This process will be iterative [*i.e.*, if additional information becomes available during the course of conducting Step 2 that indicates that the action area was not adequate for the action(s) being assessed, the action area can be revisited].

B. Step 2 (NLAA/LAA Determination):

The purpose of Step 2 is to conclude a determination of either "Not Likely to Adversely Affect" (NLAA) or "Likely to Adversely Affect" (LAA) for listed species and/or designated critical habitats within the action area. To determine whether the call for a species is an NLAA or LAA, a similar process as described above for Step 1 will be used with the exception that only endpoints relevant to the specific listed species being assessed and their habitats will be considered. Exposure values will be based primarily on fate and transport model results that assess the range of labeled uses of the pesticide (rates, methods). For aquatic exposures, PRZM/EXAMS, AgDRIFT and AGDISP will be used to predict exposure in generic habitats, referred to as bins, relevant to groups of listed species with similar habitat preferences. Exposure results for the bin most appropriate for the species being assessed will be used. For terrestrial exposures, TerrPlant, AgDRIFT, AGDISP and T-REX will be used. In this step (*i.e.*, Step 2), a refined version of T-REX that accounts for species-specific characteristics (*e.g.*, body size, diet, *etc.*), will be used.

Direct Effects (Based on Lethality):

The potential for direct effects will largely be based on those effects and endpoints that were identified in Step 1 (see Table 1) and are determined to be relevant for species and their habitats. Effects will be analyzed using a weight-of-evidence approach to make NLAA/LAA determinations. For lethality endpoints, a one in a million chance of mortality – using the most

appropriate surrogate (e.g., trout data for a listed salmonid) – will be used. For example, if the range, including critical habitat, of a listed salmonid overlaps with a ‘May Affect’ area (based on the most appropriate exposure and effects data for that particular species) where there is an estimated chance of at least one salmonid in one million dying from that exposure, this would result in a ‘LAA’ call. If enough data from appropriate surrogates are available to create a SSD for the surrogates (e.g., for example, data for several salmonid species are available to assess risks to listed salmonids), the 5th percentile of the surrogate species on the SSD will be used. If a specific surrogate is not available (e.g., only data from trout and sunfish are available to assess risks to a listed sturgeon), the most sensitive species tested in a taxon (e.g., all freshwater fish) will be used.

Indirect Effects (Based on Lethality):

The potential for indirect effects (see Table 2) will be based on the taxa that are relevant to the specific species being assessed. For potential indirect effects based on prey lethality for those species without obligate relationships, the exposure that results in a 10% effect for the 5th percentile species on a SSD will be used. If not enough data are available for a SSD, the 10% effect for the most sensitive species tested in that taxon will be used to determine the potential for indirect effects based on prey lethality.

Direct and Indirect Effects (Based on Sublethal Endpoints):

For sublethal effects to plants, the level that corresponds to the reproduction/growth NOAEC/EC₀₅ for the most appropriate surrogate species will be used to make the NLAA/LAA call. If data on a specific surrogate is not available, the most sensitive species tested in a taxon will be used (as described above). For indirect effects related to terrestrial and wetland plants (e.g., impacts to the diet or habitat of listed species based on potential effects to plants), the lowest available LOAEC or EC₂₅ from the available terrestrial plant studies will be used. The lowest available LOAEC or EC₂₅ from the available aquatic plant studies will be used to assess indirect effects associated with potential impacts to aquatic plants. Other data (e.g., incident data and other data on sublethal effects) will be qualitatively considered. For species with obligate relationships, the potential for indirect effects to the obligate species will be based on the effects endpoints identified for assessing the potential for direct effects to a species as described above (see Table 1).

For making an LAA determination based on direct effects to listed animals, the lowest available NOEC or other scientifically defensible effect threshold (EC_x) that can be linked to survival or reproduction of a listed individual will be used. For making a LAA determination for indirect effects, the LOEC or other scientifically defensible effect threshold (EC_x) for growth or reproduction will be used.

- The goal of this step is to evaluate whether an individual’s fitness (survival or reproduction) is likely compromised and whether habitat attributes are likely adversely affected for listed species.
- The NOEC and LOEC values are selected as endpoints to represent sublethal effects following chronic exposures because 1) standard chronic toxicity studies are designed to generate these values and 2) they are consistent with the goal of this step.

- Decisions on the use of EC_x values instead of NOEC and LOEC values would involve consideration of the power of the concurrent NOEC and whether there is sufficient information regarding dose-response to establish an alternative threshold with reasonable degree of confidence.
- Effect concentrations (thresholds) from growth or other sublethal endpoints will stem from studies that are relevant to environmental exposures.
- Some best professional judgment should be used to ensure selection of appropriate studies and endpoints that are relevant to the "survival and reproduction of the species in the wild" (*NAS recommendation*).
- When considering both direct and indirect effects to a listed species, sublethal effects for which quantitative linkages to apical responses have not yet been established will be incorporated as part of the weight-of-evidence approach for making NLAA/LAA determinations. This weight of evidence approach may also consider toxicity studies that are conducted at the sub-organism level (*e.g.*, on organs or cells) and that can be linked to environmentally relevant exposures. Sublethal effects data will be reviewed for relevance and data quality. The adverse outcome pathway framework can be used to structure sublethal effects data along causal pathways. Species and habitat risk hypotheses will be considered when determining relevance of data.

An overarching goal of the interim approach (Steps 1 and 2) is to collaboratively develop a streamlined consultation process that meets the needs of the FIFRA/ESA workload and integrates seamlessly into Step 3. For all of the species/critical habitats that are found to warrant NLAA determinations, based on the process described above, a streamlined consultation process will be developed, contingent on successful implementation of the other interim approach measures.

TABLE 2. Endpoints to be used in Step 2 [these values will be used to make NLAA and LAA determinations for direct and indirect effects to listed species (*e.g.*, diet, habitat) and for making adverse modification/no adverse modification determinations related to critical habitat].

Taxa on which a listed species depends	Mortality	Sublethal Effects
Birds	<p><u>Direct Effects:</u> Same as those identified in Table 1.</p> <p><u>Indirect Effects:</u> Concentration (or dose) that would result in a decrease of 10% of individuals (<i>i.e.</i> the EC₁₀). This is calculated by using HC₀₅ of SSD of LC₅₀ or EC₅₀ values and representative slope. If SSD cannot be derived, most sensitive LC₅₀ or EC₅₀ will be used.</p>	<p>For making an LAA determination based on direct effects to listed animals, the lowest available NOEC or other scientifically defensible effect threshold (EC_x) that can be linked to survival or reproduction of a listed individual will be used. For making a LAA determination for <u>indirect</u> effects, the LOEC for growth or reproduction will be used (see text for details)</p>
Mammals		
Reptiles		
Terrestrial-phase amphibians		
Aquatic-phase amphibians		
Fish		
Aquatic invertebrates		
Terrestrial invertebrates		
Aquatic plants	None	<p>Direct Effects: Same as those identified in Table 1.</p> <p><u>Indirect Effects:</u> <u>Aquatic plants:</u> Concentration equal to the</p>
Terrestrial plants		
Wetland plants		

		lowest available LOAEC and EC ₂₅ value for aquatic plants <u>Terrestrial and wetland plants:</u> Concentration equal to the lowest LOAEC and EC ₂₅ value from the available seedling emergence and vegetative vigor studies
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C. Step 3 (Jeopardy/No Jeopardy Opinion):

For all of those species/critical habitat designations found to warrant determinations of LAA, the relevant Service(s) will determine 'jeopardy' or 'no jeopardy' for species and 'adverse modification' or 'no adverse modification' for designated critical habitat (NAS' Step 3). These determinations will be based on, but not limited to, the following:

- Population models (when appropriate and available) using the same SSDs, dose-response slopes, estimates of the likely adverse impacts on a specific number of individuals within the population and other information provided in Steps 1 and 2;
- Duration of potential exposures exceeding effects thresholds; and
- Weight-of-evidence approach.

Summary of Follow up Tasks

1. Develop a common approach to weight of evidence analyses, using qualitative information for making the NLAA/LAA (and jeopardy) decisions.
2. Share information about the FESTF database and ECOS (IPaC, Critical Habitat Portal), and discuss whether/how these tools can be used as part of the interim approach to identify species and define species' ranges and critical habitats.
3. Define bins for aquatic species for use in Steps 2/3 for exposure modeling.
4. Develop guidance on the construction and use of SSDs.
5. Discuss proposal for defining agricultural pesticide use areas by aggregation of crop categories in the Cropland Data Layer (CDL) produced by USDA.

References:

National Research Council (2013). Assessing Risks to Endangered and Threatened Species from Pesticides. Committee on Ecological Risk Assessment under FIFRA and ESA, Board on Environmental Studies and Toxicology, Division on Earth and Life Studies, National Research Council of the National Academies. The National Academies Press, Washington, DC.

Interim Report to Congress

on

Endangered Species Act Implementation in Pesticide Evaluation Programs

U.S. Environmental Protection Agency, U.S. Fish and Wildlife Service, National Marine
Fisheries Service, and the U.S. Department of Agriculture

November 2014

Summary of Report

The National Academy of Sciences' report, entitled "Assessing Risks to Endangered and Threatened Species from Pesticides" was released on April 30, 2013. It contained recommendations on scientific and technical issues related to pesticide consultations under the Endangered Species Act (ESA) and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Since then the Environmental Protection Agency (EPA), the National Marine Fisheries Service (NMFS) and the Fish and Wildlife Service (FWS) (i.e., the Services) have worked to implement the recommendations. Joint efforts to date include: collaborative relationship building between EPA, NMFS, FWS, and the Department of Agriculture (USDA); clarified roles and responsibilities for the EPA, the Services, and USDA; agency processes designed to improve stakeholder engagement and transparency during review and consultation processes; two joint agency workshops resulting in interim approaches to assessing risks to ESA-listed species from pesticides; a plan and schedule for applying the interim approaches to a set of pesticide compounds; and multiple workshops and meetings with stakeholders to improve transparency as the pesticide consultation process evolves. As a result of the ongoing collaborative efforts, EPA and the Services are moving forward with developing and applying their interim approach to pesticide consultations, have completed some consultations affording species protections, and developed work products that describe changes to processes intended to streamline consultations and provide ample opportunity for stakeholder engagement as early as possible.

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Purpose of the Report

This report is intended to provide Congress with a description of the approaches and actions taken by the Environmental Protection Agency (EPA), the Fish and Wildlife Service (FWS), the National Marine Fisheries Service (NMFS), and the Department of Agriculture (USDA) (hereafter referred to as the Agencies) to 1) implement the recommendations of National Academy of Sciences' (NAS) National Research Council (NRC) report, entitled, "Assessing Risks to Endangered and Threatened Species from Pesticides" (hereafter referred to as the NRC's study), 2) ensure public participation and transparency during implementation of the recommendations from the NRC's study, and 3) minimize delays in integrating applicable pesticide registration and registration review requirements with species and habitat protections.

Background

On February 7, 2014, President Obama signed into law the Agricultural Act of 2014 (P.L. 113-79). As provided in Section 10013 of Title X – Horticulture, on the Endangered Species Act (ESA) Implementation in Pesticide Evaluation Programs, Congress required this interim report to be delivered 180 days after the Bill was signed into law and a final report in one year. The intent expressed in this provision is to keep the Agencies moving forward as they develop processes that will make it possible for EPA to comply with the ESA in a manner that maximizes resources and minimizes delays of pesticide registration and reregistration decisions under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). In addition, the provision is intended to encourage meaningful public participation, and reemphasize that all ESA-mandated Reasonable and Prudent Alternatives (RPAs) are technologically and economically feasible, that ESA-mandated Reasonable and Prudent Measures (RPMs) are necessary and appropriate, and that the Agencies have ensured public participation and transparency in the development of RPAs and RPMs.

Legal Authority

EPA regulates the distribution, sale, and use of pesticides under FIFRA. Under Section 3 of FIFRA, subject to limited exceptions, a pesticide must be registered by the EPA prior to its distribution or sale. Before EPA may register a pesticide under FIFRA, the applicant must show, among other things, that using the pesticide according to specifications "will not generally cause unreasonable adverse effects on the environment."¹

If EPA concludes that the pesticide, together with its accompanying labeling and any terms and conditions, will not cause unreasonable adverse effects on the environment, EPA grants the registration and the labeling provisions approved by EPA become the enforceable use directions for the pesticide product. Post-registration, EPA reviews and reevaluates a pesticide every 15 years to determine whether it continues to meet the FIFRA registration standard.² EPA has long stated that it will use the registration review process to address its ESA obligations for pesticide registrations and intends to do so by conducting nationwide scale effects determinations.

Under section 7(a)(2) of the ESA, all federal agencies have responsibility to insure that any action authorized, funded, or carried out by that agency is not likely to jeopardize the continued existence of any federally listed endangered or threatened species (listed species), or result in the destruction or adverse modification of designated critical habitat. Therefore, under ESA, EPA must insure that its activities in administering FIFRA are not likely to jeopardize the continued existence of any federally listed threatened or endangered species or adversely modify designated critical habitat.

¹ FIFRA defines the term "unreasonable adverse effects on the environment" to mean: "(1) any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide; or (2) a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard under section 408 of the Federal Food, Drug, and Cosmetic Act."

² Due to concerns that much of the safety data underlying pesticide registrations becomes outdated and inadequate, FIFRA Section 4 requires that registrations be reviewed every 15 years and requires EPA to reregister all pesticides that were registered before 1984. The goal is to update labeling and use requirements and reduce potential risks associated with older pesticide active ingredients -- those first registered when the standards for government approval were less stringent than they are today. This comprehensive reevaluation of pesticide safety in light of current standards is critical to protecting human health and the environment.

Regulations implementing Section 7 of the ESA require that federal agencies initiate “consultation” with the appropriate Service(s) on certain actions that “may affect” ESA-listed species or designated critical habitat. The appropriate Service depends on the agency’s action, the ESA-listed species potentially affected by that action, and the Service responsible for administering consultations for the listed species potentially affected. The Services conclude a formal consultation by issuing a Biological Opinion that addresses the federal agency action considered during consultation. The appropriate Service determines whether the proposed action assessed in the Biological Opinion is likely to jeopardize the continued existence of any ESA-listed species, or destroy, or adversely modify the designated critical habitat of such species. If the FWS, or NMFS, determines from its assessment that a proposed action is likely to jeopardize the continued existence of the species, or destroy or adversely modify critical habitat, it must provide the federal agency with RPAs to the action, if any exist, that the Service determines will preclude likely jeopardy and destruction or adverse modification of critical habitat. If the relevant Service concludes that take (*i.e.*, harass, harm³, pursue, hunt, shoot, wound, kill, trap, capture, or collect any threatened or endangered species) will not violate ESA section 7(a)(2), the Service provide the federal agency with an incidental take statement (ITS). The ITS identifies the amount or extent of take, RPMs that minimize the impact of take, and implementing terms and conditions. Incidental take that occurs when the agency action is conducted in compliance with the implementing terms and conditions is exempt from statutory or regulatory prohibitions of take that would otherwise apply.

It should be noted that USDA has no formal role in the consultation process. USDA’s role is to provide pesticide use and usage data as well as information on agricultural production practices. The National Agricultural Statistics Service (NASS) is providing assistance with the appropriate use of the Crop Data Layer and other geospatial information related to the location of agricultural crops.

³ Harm is further defined in 50 CFR Part 222

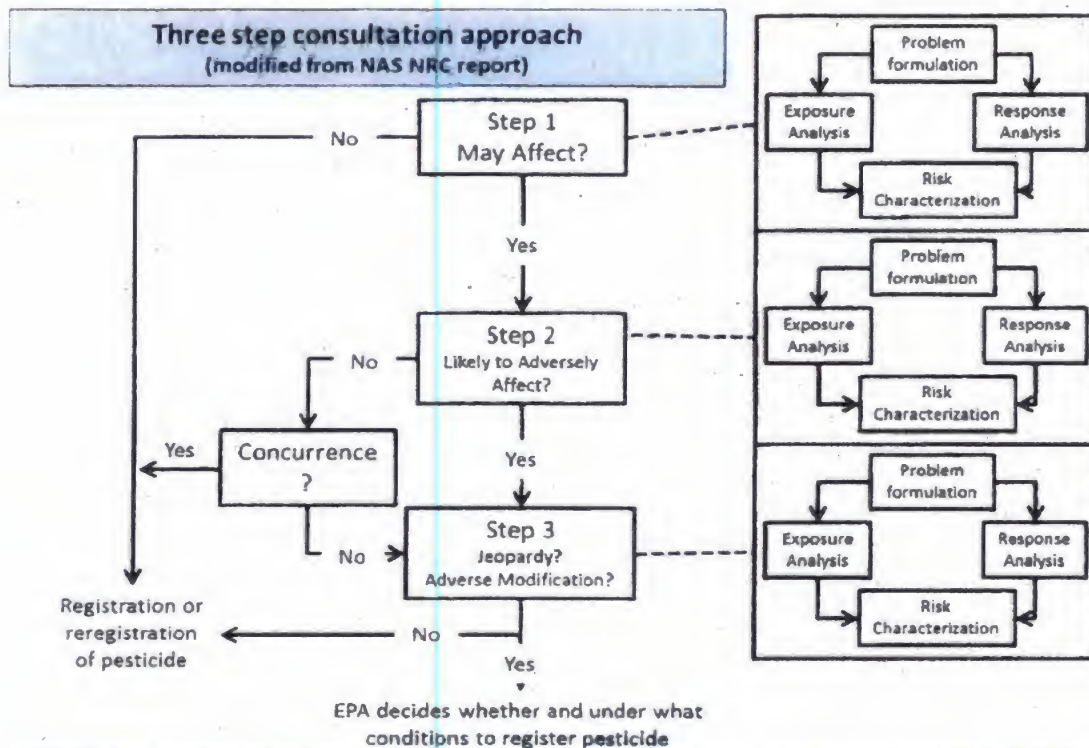
National Academy of Sciences Study Implementation

On March 10, 2011, the Agencies requested that the NRC convene a committee of independent experts. "The committee was asked to evaluate EPA's and the Services' methods for determining risks to ESA-listed species posed by pesticides and to answer questions concerning the identification of the best scientific data, the toxicological effects of pesticides and chemical mixtures, the approaches and assumptions used in various models, the analysis of uncertainty, and the use of geospatial data."⁴ Specifically, the committee was asked to evaluate the protocols used by EPA and the Services to review the best available scientific methods for projecting these effects and consider options for the development of any additional methods that are likely to be helpful, to consider the scientific information available to assess the potential effects of mixtures and inert ingredients, to consider the selection and use of uncertainty factors to account for lack of data and how the choice of those factors affects estimates of uncertainty, and to advise on the use of models to assist in analyzing the effects of pesticide use and on the use of geospatial information and datasets in assessing the risk to endangered and threatened species from pesticides.

On April 30, 2013, the NRC provided their recommendations to the Agencies in the form of a report⁵. Upon receipt of the study report, the Agencies began a joint review and discussion of the recommendations and developed a plan for their implementation. As part of the implementation plan, the Agencies determined which recommendations could be implemented immediately, which recommendations would take longer to implement, and which recommendations required additional interagency discussions. The Agencies are implementing the NRC study's recommended three-step consultation approach, shown below.

⁴ Assessing Risks to Endangered and Threatened Species from Pesticides (National Research Council, 2013; http://www.nap.edu/catalog.php?record_id=18344

⁵ Ibid.



NOAA FISHERIES



- Step 1 ('No Effect/May Affect' determination) - EPA makes the "no effect/may affect" determination independently of the Services at Step 1. If EPA determines that a pesticide's registration, or reregistration, will have "no effect" on ESA-listed species it may move forward with a pesticide's registration, or reregistration, without consulting with the Services. If EPA determines that a pesticide's registration, or reregistration "may affect" ESA-listed species, the pesticide's potential impact on ESA-listed species must be considered under Step 2. The 'No Effect/May Affect' determination will largely be based on the overlap of the action area with the species' ranges and designated critical habitats (i.e., any species or critical habitat that overlaps with the action area will be considered a 'May Affect'). The action area will be defined by identifying pesticide use areas (i.e., the pesticide use footprint) based on currently registered labeled uses (i.e., the Action). In addition, the

action area will include a footprint that extends beyond the use sites to incorporate off-site transport including pesticide spray drift and runoff.

- Step 2 ('Not Likely to Adversely Affect (NLAA)/Likely to Adversely Affect (LAA)' determination) – EPA determines whether a pesticide's registration, or reregistration is "likely to adversely affect", or "not likely to adversely affect" ESA-listed species. When EPA determines that an effect is "not likely to adversely affect" they must seek concurrence from the Services. When EPA determines that an effect is "likely to adversely affect," EPA and the Services enter into formal consultation, and Step 3 is initiated. To determine whether the call for a species is an NLAA or LAA, a similar process as described above for Step 1 will be used with the exception that only endpoints relevant to the specific listed species being assessed and their habitats will be considered. Exposure values will be based primarily on fate and transport model results that assess the range of labeled uses of the pesticide (rates, methods). For aquatic exposures, PRZM/EXAMS, AgDRIFT and AGDISP will be used to predict exposure in generic habitats, referred to as bins, relevant to groups of listed species with similar habitat preferences. Exposure results for the bin most appropriate for the species being assessed will be used. For terrestrial exposures, TerrPlant, AgDRIFT, AGDISP and T-REX will be used. In this step (i.e., Step 2), a refined version of T-REX that accounts for species-specific characteristics (e.g., body size, diet, etc.), will be used.
- Step 3 ('Jeopardy/No Jeopardy' determination and "Adverse Modification/No Adverse Modification" on effects to designated critical habitat(s) determination) – For all of those species/critical habitat designations found to warrant determinations of LAA, the relevant Service(s) will determine 'jeopardy' or 'no jeopardy' for species and 'adverse modification' or 'no adverse modification' for designated critical habitat. These determinations will be based on a weight-of-the-evidence approach that evaluates species and habitat risk hypotheses and associated lines of evidence. A variety of tools

will be employed to assess the population and species responses including but not limited to population modeling (when appropriate data are available on species and habitat use).

The Agencies are holding a series of internal workshops to develop procedures and methodologies to address NRC study's recommendations that cannot be implemented immediately, but that are considered to be short-term, or long-term goals. The Agencies conducted their first workshop during the week of August 5, 2013, in which interim approaches for estimating risks to listed species from pesticides were developed jointly by the Agency scientists. In keeping with the NRC's study recommendations, the result is a streamlined consultation process that relies on best available data to inform an ecological risk assessment based on robust quantitative and qualitative analyses. The white paper describing the interim approaches entitled, "Interagency Approach for Implementation of the National Academy of Sciences Report" (11/13/2013) is available at the following website: <http://www.epa.gov/oppfead1/endanger/2013/nas.html>

The white paper explains in more detail the procedures and methodologies that will be used in Steps 1, 2, and 3, including how a pesticide's "action area"⁶ will be determined in Step 1 and what constitutes effects thresholds⁷ in Steps 1 and 2. The white paper emphasizes the importance of using quantitative analysis whenever possible and explaining the rationale supporting a qualitative analysis, and states that the ECOTOX toxicology database⁸ supplemented with information from the Services⁹ will generally constitute best available data for toxicity. The white paper explains that as part of

⁶ Action area means all areas to be affected directly or indirectly by the Federal action and not merely the immediate area involved in the action (50 CFR § 402.02). (<http://www.fws.gov/endangered/what-we-do/faq.html>)

⁷ Effects thresholds are derived from available, scientifically valid toxicity data. They are designed to be conservative and to represent the risk management goals of the ESA, which are focused on effects to an individual's fitness.

⁸ ECOTOX is a comprehensive database, which provides information on adverse effects of single chemical stressors to ecologically relevant aquatic and terrestrial species. ECOTOX includes more than 40,000 test records covering 5,900 aquatic and terrestrial species and 8,400 chemicals. The primary source of ECOTOX data is the peer-reviewed literature with test results identified through comprehensive searches of the open literature (<http://cfpub.epa.gov/ecotox/>).

⁹ This may include peer-reviewed studies not included in the ECOTOX database and other relevant toxicity studies including those generated by city, county, state, and federal entities.

implementing Steps 1 and 2, predictive models will be used to estimate pesticide concentrations in soil, air, and water and environmental exposures to them, as well as targeted and ambient water quality monitoring. Formulated products with more than one active ingredient, tank mixes, and environmental mixtures will largely be considered qualitatively.

The white paper also identified several follow-up tasks related to the NRC study's recommendations that are considered to be short-term, or long-term goals that will be developed further by the Agencies, specifically:

1. Develop a common approach to weight of evidence (WOE) analyses, using quantitative and qualitative information for making NLAA/LAA (and jeopardy and adverse modifications of critical habitat) decisions.
2. Share information about the FIFRA Endangered Species Task Force (FESTF) database and the U.S. Fish and Wildlife Services' Environmental Conservation Online System (ECOS) and discuss whether/how these tools can be used as part of the interim approach to identify species and define species' ranges and critical habitats. Within ECOS, there are various modules that the agencies are exploring to gather or store species information, including the Information, Planning, and Conservation System (IPaC), the Critical Habitat Portal, and the Threatened and Endangered Species System (TESS). These three modules include various scales of geospatial data for species ranges (e.g., county-level, areas of influence) and critical habitat.
3. Describe "bins" (i.e., type of water body) for aquatic species for use in Steps 2 and 3 for exposure modeling. The water body may vary by depth, width, and flow; it may be static, flowing, estuarine, intertidal, subtidal, or offshore marine.
4. Develop guidance on the construction and use of species sensitivity distributions (SSDs).

5. Discuss proposal for defining agricultural pesticide use areas by aggregation of crop categories in the Cropland Data Layer (CDL) produced by USDA.

The interim approaches, including the follow-up tasks, were presented to the public during a workshop on November 15, 2013. Presentation materials from the stakeholder workshop are available at the following website:

<http://www.epa.gov/oppfead1/endanger/2013/nas.html>

The Agencies have been working continuously since the release of the NRC's study on all of these areas, simultaneously. The expectation is that these additional approaches can be incorporated into the risk assessment process on a "day forward approach". This means that our shared scientific approaches, once fully developed, will be applied to pesticide reviews from that point in time and going forward rather than reworking assessments and decisions already completed.

The Agencies held a second internal workshop during the week of May 5, 2014 to continue development of joint interim approaches for assessing risks to ESA-listed species from pesticides, and to deliberate on the follow-up tasks identified in the white paper. As a result of this workshop, the Agencies have developed a draft annotated outline for EPA's ESA-listed species' risk assessments, or biological evaluations.

Progress towards implementing the NRC study's recommendations considered to be short-term or long-term goals includes:

1. Weight-of-evidence analysis being developed – Developing a common approach to weight-of-evidence analysis that includes an explanation of how all of the information (quantitative and qualitative) was used to draw and support conclusions. Agency scientists have drafted guiding principles that will be further developed in concert with the national-level consultations discussed below. EPA and the Services are working together to develop a

WOE approach that can be used for the species-specific determinations, and are planning on using WOE in Step 2. We have not yet had discussions on using WOE at Step 3.

2. Geospatial data being defined - Identifying sources of geospatial data to map the locations of ESA-listed species, and their designated critical habitat and ranges, and to map crop locations for use in defining a pesticide's action area (Step 1 in the NRC study). The Agencies are pursuing sources of this information considered "best available data" through various sources, including two pesticide industry task forces: Federal Endangered Species Task Force (FESTF) and Generic Endangered Species Task Force (GESTF).
3. The Agencies met with FESTF on November 25, 2013 and again on March 27, 2014. During the November meeting, FESTF representatives provided the Agencies with an overview of their databases and sources of their data. During the March meeting, FESTF representatives provided a more detailed comparison of ESA-listed species' locations from individual sources, and demonstrated an information management system through which species location maps from individual sources could be compiled, contrasted, and compared. FESTF has begun delivery of species range maps that include aggregated available geospatial information (e.g., including critical habitat information from ECOS) to the FWS field offices for use in the development of vetted listed species ranges for the initial pesticide consultations. Once the field offices have completed their review and refinement of the range maps, they will be sent to FWS Headquarters for review prior to delivery to EPA/FESTF as appropriate.
4. The Agencies met with GESTF on January 15, 2014 to discuss their efforts to map crop locations using NASS CDL data. Based on the information and understanding of available data and information on ESA-listed species locations, designated critical habitat and range, and cropping patterns gained from these meetings, the Agencies have drafted an approach for establishing

the action area and determining whether the action may affect ESA-listed species or designated critical habitat, i.e., Step 1 of the NRC's study recommendations. Currently, GESTF is investigating approaches to mapping non-agricultural crops. GESTF expects to share their findings with the EPA by the end of the end of 2014.

5. Exposure modeling being developed - EPA is developing a nationwide pesticide aquatic exposure model that defines the magnitude and extent of pesticide concentrations in water that is spatially explicit and captures seasonal and yearly variations. The outputs of this spatial aquatic model will provide a better definition of the aquatic spatial footprint of pesticide exposures in the action area. EPA just completed a pilot version of the model for the Midwest and is in the process of expanding to the entire country. On March 24, 2014, EPA provided an update on the model at a public workshop. This workshop provided an opportunity for stakeholders to provide technical and scientific feedback on the model. On August 13, 2014, a presentation was made to the American Chemical Society (ACS) meeting.
6. Species Sensitivity Distributions (SSDs) and population modeling being developed - Different methods for deriving species sensitivity distributions have been reviewed and will be applied to the initial consultations that the EPA and Services will conduct in the coming months. The Services and EPA are currently developing population modeling through monthly discussions with academic and government experts. EPA's Office of Research and Development and Office of Pesticide Programs are developing general and species-specific population models. Species sensitivity distributions will be for procedures separate from population modeling.

Based on recent settlement agreements as part of ongoing litigation against EPA and the Services (i.e., Northwest Center for Alternatives to Pesticides (NCAP) v. EPA, NCAP v. NMFS, and Center for Biological Diversity (CBD) v. FWS), the Agencies have agreed to

coordinate completion of nationwide consultations for five pesticides, carbaryl, chlorpyrifos, diazinon, malathion, and methomyl. The dates provided for completion of consultation in those settlements is December 2017 for chlorpyrifos, diazinon, and malathion, and December 2018 for carbaryl and methomyl. The Agencies are beginning to implement the interim approaches for chlorpyrifos, diazinon, and malathion using the annotated outline drafted during the May 2014 workshop.

In addition, three teams of interagency scientists have been formed and are currently working to complete effects determinations (i.e., Steps 1 and 2) for chlorpyrifos, diazinon, and malathion. All three teams have developed SSDs for fish, aquatic invertebrates, and birds and are currently reviewing other toxicity data available in the literature. EPA has developed an analytical approach that identifies and groups data (e.g., endpoints specific to family, species and endpoints) that allows risk assessors to easily access and review relevant toxicity data. Subgroups have been formed to continue to develop methods that may be used by all three chemical teams. These subgroups are focused on problem formulation development, aquatic exposure methodology, and probabilistic methodology. The problem formulation subgroup is identifying critical information that should be included in this portion of the written assessments. The aquatic exposure group is working to develop model assumptions and simulate the diverse aquatic habitats that are necessary for listed species, and the probabilistic subgroup is considering what questions could be addressed with probabilistic methods.

Meaningful Public Participation and Transparency

Existing processes for registration, registration review, and consultation provide multiple opportunities for stakeholder engagement. Although federal law only requires limited public participation in the pesticide registration process, EPA's Pesticide Program began implementing a public participation process for certain registration actions in October 2009. The public participation process for registration actions provides a meaningful

opportunity for the public to comment on major registration decisions at a point in the registration process when comprehensive information and analysis are available. The Agency intends to use the outlined public participation process for the following types of applications: new active ingredients; first food use, first outdoor use; first residential use; and other actions of significant interest.

The current post-registration review process – known as registration review -- was created by section 3(g) of FIFRA and mandates that EPA review pesticides not less often than every 15 years. Under section 3(g)(1)(A)(ii), EPA has established procedures for registration review in its final rule published in the Federal Register (71 FR 45,732, Aug. 9, 2006, as amended at 73 FR 75595, Dec. 12, 2008) and codified at 40 CFR Part 155 Subpart C – Registration Review Procedures. Under the procedures established per 40 CFR part 155 Subpart C, three specific time points have been identified for public notification and comment during registration review: 1) initiation of a pesticide's reevaluation, 2) when a draft risk assessment has been conducted, and 3) for a proposed registration review decision. In addition to the public review and comment periods outlined above, EPA may meet with stakeholders at any time during registration review, either through Agency initiation, or stakeholder request, to discuss an ongoing registration review (40 CFR Part 155.52).

EPA's Endangered Species Protection Program (ESPP) is the EPA program for addressing the requirements of the ESA in connection with EPA's implementation of FIFRA. Announced in a November 2, 2005, Federal Register Notice, the 2005 ESPP document¹⁰ outlines three opportunities for public input and participation during registration review: 1) prior to a "may affect" determination by EPA, 2) when identifying potential mitigation if a risk assessment identifies a listed species concern, and 3) prior to issuance of a Biological Opinion to EPA by the Services. Under the ESPP, EPA will generally engage the public in each of these three stages of its ESA-related work. The first and second opportunity for public review and comment meld with existing

¹⁰ <http://www.gpo.gov/fdsys/pkg/FR-2005-11-02/pdf/05-21838.pdf>

procedures established for registration review. These existing opportunities for public input have been strengthened and enhanced through process improvements jointly developed by the Agencies as described below.

In response to stakeholders' concerns expressed regarding a lack of transparency surrounding pesticides consultations, the Agencies have been seeking input from stakeholders on how to improve opportunities for their engagement in our processes. Specifically, stakeholders expressed the need for increased access to the decision-making process to give states and other stakeholders increased opportunities to provide relevant data for consideration during consultation, and the need for adequate time for public review and comment.

As mentioned above, the interim approaches developed by the Agencies in the summer and fall of 2013 were presented to the public during a workshop on November 15, 2013. On April 22, 2014, at the request of stakeholders, the Agencies held a public workshop to provide a forum for stakeholders to present scientific and technical feedback on the interim approaches. Representatives from the pesticide industry and non-governmental organizations attended the workshop and provided feedback. The scientific and technical presentations are available in the public docket (EPA-HQ-OPP-2014-0233) which can be accessed through www.epa.gov/pesticides/oppfead1/endanger/2013/nas.html. The Agencies are continuing to consider the information provided during the workshop as to how it might improve and facilitate listed species consultations. As described in more detail below in this report, public workshops, such as those held in November 2013, April 2014, and October 2014, further the Agencies' goal of developing a consultation process for pesticide impacts on listed species that is efficient, inclusive, and transparent.

However, the Agencies' efforts to improve transparency for pesticide consultations began earlier. Since 2011, the Agencies have organized and participated in meetings and workshops with stakeholders affected by pesticide consultations. The intention of the outreach efforts was to identify improvements to the registration review and consultation processes that would more fully involve stakeholders. Our intention in organizing and

holding these public meetings has been to obtain as much input as possible from stakeholders affected by ESA-related work and decisions under FIFRA.

A workshop organized with the Minor Crop Farmer Alliance addressing grower concerns was held in Denver, Colorado in May 2011. There was general agreement that information was needed to clarify and confirm product labeling information, identify where crops are grown, and that growers need to be engaged early and often. The meeting minutes and materials provided for and discussed at the workshop can be found at:

<http://www.ffva.com/imispublic/Content/NavigationMenu2/AgResources/Aglinks/Meetingmaterials/default.htm>. Copies of the individual presentations can be found on the following websites: Florida Fruit & Vegetable Association, www.ffva.com; and the California Citrus Quality Council, www.calcitrusquality.org.

Meetings were held in July and September 2011 with the Pesticide Program Dialogue Committee and its subgroup, the Pesticide Registration Improvement Act Process Improvements Workgroup. Members of these fora represent a variety of stakeholders including pesticide registrants, growers, states, and non-governmental organizations. These discussions centered on opportunities for public participation on ESA-related work under registration review and explored the appropriate timing during registration review for initiating consultation with the Services. The meeting minutes can be found at: <http://www.epa.gov/oppfead1/cb/ppdc/pria/index.html#meetings>.

In response to the stakeholder feedback gained in 2011, the Agencies prepared and proposed for public comment the paper entitled, "Enhancing Stakeholder Input in the Pesticide Registration Review and ESA Consultation Processes and Development of Economically and Technologically Feasible Reasonable and Prudent Alternatives" (hereafter referred to as the Stakeholder Paper). The Agencies finalized the Stakeholder Paper in March 2013; it can be found at www.regulations.gov in the following docket: EPA-HQ-OPP-2012-0442. The processes described in the Stakeholder Paper supersede similar provisions in the 2005 ESPP document.

The Stakeholder Paper sets the stage for enhanced public engagement and describes changes to the Services' and EPA's review processes intended to enhance opportunities for stakeholders to provide input during review of pesticide registrations and consultations. It begins by emphasizing the value of improved coordination across the Agencies, a key recommendation of the NRC's study. Plans to reach out at the earliest point to pesticide users potentially affected to discuss the technological and economic feasibility of draft RPAs and RPMs intended to avoid jeopardy and adverse modification to critical habitat are included. The proposal describes the process by which stakeholders' comments on RPAs will be received by EPA and provided to the Services, who will then prepare a document to be included in the administrative record of the consultation explaining how comments were considered, and if appropriate, how the final biological opinion was modified to address the comments. The Services will provide the document to EPA, and both the Services and EPA will make the document available to the public upon request. The Agencies believe these changes provide clarity and transparency to Section 7 ESA consultations for pesticides and result in improved ESA pesticide consultations.

The Stakeholder Paper also describes "Focus" meetings, now being held at the start of registration review for pesticide active ingredients. This change brings the affected stakeholders into EPA's review process at the earliest point of a pesticide's registration review cycle. The Stakeholder Paper describes EPA's and the Services' agreement to initiate formal consultations at a later stage in the review process; consulting later in the registration review process allows EPA to develop more refined ecological risk assessments and to engage affected stakeholders in discussions throughout EPA's review process resulting in more focused consultation packages inclusive of any agreed upon mitigation for ESA-listed species. It recognizes USDA's valuable relationships with the agricultural community that provide a critical link between EPA's expertise on pesticides and the Services' expertise on listed species' locations, status and biology. The process changes described in the proposal have the potential to maximize the opportunity to effect changes that provide protections for species and their designated critical habitat,

lessen the impacts on agriculture, and narrow the scope of any necessary ESA consultations. USDA attends Focus meetings regularly, and the Services attend when warranted.

Currently, EPA uses the web application "Bulletins Live!" to set forth geographically-specific pesticide use limitations for the protection of threatened and endangered species and their designated critical habitat. "Bulletins Live!" can be found at <http://www.epa.gov/opptead1/endanger/bulletins.htm>. EPA is upgrading to "Bulletins Live! Two" (BLT). The upgrades will move away from static county maps to an interactive map such as Bing™, or Google Earth™. BLT will be geo-coded making it possible for users to zoom in and out and focus on their area of interest, conduct searches for products (by name and EPA registration number) in addition to active ingredients, and download data. These upgrades are intended to make the web application setting forth species protections more user friendly for growers likely to be impacted by species protections.

By following the process outlined in the Stakeholder Paper, the following examples show positive outcomes resulting from enhanced stakeholder engagement during 1) consultations resulting from litigation, and 2) registration review.

Litigation Consultations

Rozol - Rozol™ is a rodenticide used to control black-tailed prairie dogs. The consultation was the result of a lawsuit, in which the court-ordered EPA to cancel Rozol's™ registration. EPA and FWS worked collaboratively with stakeholders (registrants) very early during the consultation to identify conservation measures that protect species and their critical habitat. Early mitigation termed "conservation measures" was agreed to prior to the final biological opinion. Incorporation of conservation measures protecting species and their designated critical habitat resulted in a "no jeopardy" conclusion, making RPAs unnecessary. Technologically and economically feasible RPMs were developed collaboratively between FWS, EPA, and the registrant. The consultation was completed efficiently and species protections put in place quickly.

Kaput - Kaput™ is a rodenticide used to control black-tailed prairie dogs which was also the subject of a lawsuit. The Agencies built upon their success from the Rozol™ consultation and applied the same early stakeholder engagement strategy to implement risk mitigation measures that would support a “no jeopardy” conclusion, negating the need for RPA, but achieve species protections through negotiated RPMs.

Thiobencarb - Thiobencarb is one of the pesticides included in the lawsuit related to pesticide impacts on Pacific Northwest salmonids. Early engagement between NMFS, EPA, the California Department of Pesticide Regulation (CDPR), the registrant, and the California Rice Commission allowed EPA and NMFS to develop an implementation plan for thiobencarb use on rice in California. NMFS considered and used existing state programs to mitigate risks to species and protect designated critical habitat. This resulted in a “no jeopardy” conclusion. RPM were based on existing state programs and developed in collaboration with EPA, CDPR, and NMFS. EPA is working with the registrant, state, and impacted growers to implement the RPM via endangered species bulletins. The draft bulletins were made available to affected stakeholders for public comment.

Ongoing pesticide consultations regarding salmonids - Diflubenzuron, propargite, and fenbutatin-oxide are three of the pesticides included in the lawsuit related to pesticide impacts on Pacific Northwest salmonids. EPA and NMFS worked with the registrants to identify pesticide uses that posed the greatest risks to salmonids. Registrants proposed several label modifications to labels to reduce risk to the species. EPA is now working with the registrants to incorporate the agreed upon mitigation measures into pesticide product labels. The final Biological Opinion is scheduled for completion in December 2014.

Registration Review

Starlicide - Starlicide™ is an avicide used mainly on rice, typically in the form of bait. It is currently undergoing registration review; and consultation has not been initiated. It

provides an example of positive outcomes from early stakeholder engagement prior to consultation. In the interest of reducing non-target exposure, EPA met regularly with USDA's Animal and Plant Health Inspection Service (APHIS) and the US Rice Federation to discuss ways to minimize exposure and reduce costly data requirements. The US Rice Federation suggested tilling the soil after the application/bait period would bury leftover bait, making it less accessible to non-targets. This would be a practical mitigation measure that is technologically and economically feasible for the rice use, and may work for some of the other broadcast uses as well. The goal of these outreach efforts is to eliminate or limit the potential for non-target exposures from the rice use and other broadcast uses, subsequently negating the need for the majority of the data requirements for Starlicide™. This modification will be reflected in the consultation EPA initiates with FWS as it works to complete registration review. The Agencies are working towards this kind of successful outcome through collaborative dialogue with stakeholders resulting in technologically and economically feasible mitigation measures, which when implemented have the dual benefits of precluding the need for expensive data requirements, and reducing, or eliminating concerns for listed species.

Gas cartridges - Gas cartridge products are used to control a variety of pests. It is currently undergoing registration review; and informal consultation has been initiated. It provides an example of achieving risk mitigation for some listed species through informal consultation. EPA and APHIS have worked closely together and developed a set of risk mitigation measures that build upon work already completed under previous consultations with FWS. APHIS has agreed to place the risk mitigation measures on their product labels narrowing the scope of consultation. The comment period on EPA's proposed interim decision is now closed. EPA is considering those comments and formulating the interim decision.

Silica - Silica (Diatomaceous Earth) is an insecticide that is currently undergoing registration review. EPA and FWS successfully completed informal consultation on 57 listed species that may be directly or indirectly affected by the use of silica. FWS

concluded with EPA's determination that silica "May affect, but is not likely to adversely affect" these species.

All of the examples described above reflect the benefit of working closely with stakeholders prior to initiation of consultation and sharing the conclusions of past consultations, which allows EPA to build upon work done for existing consultations. These positive outcomes underscore the importance of early engagement with stakeholders, consideration of existing consultations, state programs and state co-regulators, and flexibility.

Registration

EPA recently registered the herbicide, Enlist Duo, containing 2,4-D and glyphosate. The product is for use in controlling weeds in corn and soybeans genetically-engineered to tolerate 2,4-D and glyphosate. EPA scientists used highly conservative and protective assumptions to evaluate ecological risks for the new uses of 2,4-D in Enlist Duo. The assessments confirm that these uses meet safety standards for pesticide registration, and as approved, will be protective of non-target species, including endangered species. To minimize potential exposures of non-target species, use restrictions to minimize drift include 30-foot in-field "no spray" buffer zones around the application areas, no pesticide application when the wind speed is over 15 mph, and only ground applications are permitted. In addition, the approved formulation is less prone to drift than other forms of 2,4-D. EPA's final regulatory decision document is available in EPA docket EPA-HQ-OPP-2014-0195.

Anticipating, Minimizing, and Resolving Delays

In an effort to narrow and further streamline the pending consultations for ESA, EPA is compiling information on existing consultations for the approved use of pesticides on federal lands. By building on existing consultations that have already been completed for certain pesticides, EPA believes that significant efficiencies can be introduced into the nationwide pesticide consultations that will occur during registration review. In addition,

RPAs and RPMs identified in previous biological opinions can serve as the foundation for label clarifications and early risk mitigation since previous consultations have identified such measures as being helpful to endangered species. EPA's intent is to use and build upon those existing consultations between the Services and the other federal agencies. By using the results on consultations already completed by other federal agencies, EPA will reduce duplication of effort and save resources. EPA prepared and sent letters to the Bureau of Land Management, Department of Defense, Forest Service, Tennessee Valley Authority, Bureau of Indian Affairs, National Park Service, FWS, Department of Energy, and the Bureau of Reclamation requesting biological opinions, points of contact, lists of species on federal lands, chemicals approved for use on federal lands, and data. EPA is organizing the responses and information from the federal agencies. Once organized, this information will be reviewed and captured for use in future consultations.

Litigation constrains resources. Agency staff working on litigation-driven, species-specific complaints are diverted from working towards completing national-level consultations. The agencies have worked with litigants to align lawsuits so that the agencies could focus on national level consultations on all ESA-listed species rather than focus on single species, or a small subset of species in smaller geographical areas. The plaintiffs appreciate that the Agencies have limited resources, but have expressed their concern that the Agencies address pesticides that pose the most threat to listed species, first.

In the interest of preventing litigation and addressing plaintiffs concerns, EPA continuously dialogues with potential plaintiffs and employs a 3-pronged strategy that is intended to protect listed species and their designated critical habitat by focusing resources on areas where we can achieve the most protections. First, EPA will undertake the majority of its ESA consultation work through registration review. This allows EPA to focus on chemicals with higher risk, i.e., the "worst first", resulting in the greatest potential benefits for listed species while addressing plaintiff concerns, thus, minimizing potential future litigation. Consistent with the interagency "shared scientific approaches"

and "day forward approach," we will phase in the interim scientific approaches over time. EPA, FWS, and NMFS will apply the interim measures to initial consultations and, based upon the experience gained with these approaches as well as any new science that may develop, modify procedures as appropriate.

Secondly, EPA intends to complete Overview Document-compliant endangered species assessments for new herbicide tolerant crop uses. An assessment that is Overview Document-compliant follows the procedures and methods described in the Overview Document. Currently, the Overview Document is the basis for all ecological assessments for all chemicals other than chlorpyrifos, diazinon, malathion, carbaryl, and methomyl. EPA will complete these effect determinations as resources allow. To maximize impact within these resources, it is likely that the initial registrations will not be nationwide in scope, and to the extent practical will focus on situations where EPA can make "no-effect" decisions. The Overview Document can be found at the following link: <http://www.epa.gov/oppfead1/endanger/consultation/ecorisk-overview.pdf>. As mentioned above, EPA recently registered the herbicide, Enlist Duo, containing 2,4-D and glyphosate.

Thirdly, EPA will provide information that compares the potential hazards of the new active ingredients to already registered pesticides with similar modes of toxicity and the same use patterns. This will allow stakeholders to compare the relative toxicity of the proposed registration to available alternatives. We believe that older, currently registered chemicals typically have the potential to pose greater risks to ESA-listed species than do the newer, generally safer pesticides being introduced into the marketplace today, and that the comparative hazard information will illustrate this to all stakeholders. This additional hazard information contributes to transparency and promotes good communication with the public, improves relationships and trust with our stakeholders, and maximizes the potential to minimize litigation and prevent delays.

Conclusion

The Agencies have developed a joint, highly robust process to address pesticide consultations under the ESA. We are collaborating on developing interim approaches to apply to national-level risk assessments for pesticides and coordinating our responses on litigation. The scientific procedures and methodologies developed as part of the interim approaches are the best that have ever been developed for ESA-listed species-pesticide consultations. EPA and the Services will continue working towards incorporating the NRC study's recommendations over the coming months to strengthen even further the foundation behind these assessments. EPA and the Services are committed to scientifically sound risk assessments resulting in protections for ESA-listed species that do not unnecessarily hinder agriculture. EPA and the Services are committed to maintaining a robust dialogue with all of our stakeholders to ensure transparency throughout the pesticide consultation process. Regular, meaningful communication and collaboration between the Agencies' management and scientific staff is important to maintaining our current momentum and success.

Positive outcomes from the Agencies' joint efforts include: some early successes on litigation-driven consultations affording species protections for some chemical/species combinations, the Stakeholder Paper, interim approaches to pesticide risk assessments for listed species, interagency workshops, public comment periods on important papers and work products, and meetings open to the public to keep stakeholders informed of our progress as we move forward. In addition, EPA and the Services are working together on negotiations with plaintiffs to address our agency-specific lawsuits. Positive outcomes from this transition include negotiated settlements and extensions on ongoing litigation, allowing EPA and the Services to devote time and resources to implementation of the recommendations provided in the NRC's study and to deliver nationwide assessments for listed species.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

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Gary Frazer
Assistant Director for Endangered Species
U.S. Fish and Wildlife Service
1849 C Street NW
Washington, D.C. 20204

Donna Wieting
Director, Office of Protected Resources
NOAA National Marine Fisheries Service
1315 East-West Highway
Silver Spring, MD 20910

Dear Mr. Frazer and Ms. Wieting:

The Office of Pesticide Programs (OPP), U.S. Environmental Protection Agency (EPA) respectfully requests the initiation of Endangered Species Act (ESA) section 7(a)(2) formal consultation under 50 CFR Part 402.46, Optional Formal Consultation Procedures for FIFRA Actions. This nation-wide consultation request addresses the potential effects of pesticides registered under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) and containing the active ingredients diazinon, chlorpyrifos, and malathion to all Federally listed and proposed endangered and threatened species (hereafter referred to as listed species) and their designated critical habitats.

Our biological evaluations, which were developed in collaboration with the U.S. Fish and Wildlife Service and the National Marine Fisheries Service (collectively, the Services) as described further below, resulted in determinations that the use of pesticides containing diazinon, chlorpyrifos, and malathion are likely to adversely affect (LAA) one or more individuals for a number of listed species and their designated critical habitat. A summary of the effects determinations for listed species and designated critical habitat for the three chemicals are provided below in Tables 1 and 2, respectively. Further details on the number of LAA, not likely to adversely affect (NLAA) and no effect determinations by taxon (e.g., fish, mammals, birds, etc.) are provided in Section 4, Table 4.1 of the final biological evaluations for the three pilot chemicals [<https://www.epa.gov/endangered-species/implementing-nas-report-recommendations-ecological-risk-assessment-endangered-and>].

Table 1: Listed Species Effects Determinations*

Chemical	No Effect	Not Likely to Adversely Affect	Likely to Adversely Affect
Diazinon	114 (6%)	284 (15%)	1437 (78%)
Chlorpyrifos	16 (1%)	41 (2%)	1778 (97%)
Malathion	16 (1%)	41 (2%)	1778 (97%)

*1835 listed species were evaluated; the percentage of the total number is listed in parentheses.

Table 2: Designated Critical Habitat Effects Determinations*

Chemical	No Effect	Not Likely to Adversely Affect	Likely to Adversely Affect
Diazinon	83 (10%)	326 (41%)	385 (48%)
Chlorpyrifos	0 (0%)	14 (2%)	780 (98%)
Malathion	0 (0%)	14 (2%)	780 (98%)

*794 designated critical habitats were evaluated; the percentage of the total number is listed in parentheses.

The biological evaluations for diazinon, chlorpyrifos, and malathion were conducted consistent with the interim scientific methods for national-level pesticide ESA assessments developed collaboratively by EPA and Services (<https://www.epa.gov/sites/production/files/2015-07/documents/interagency.pdf>) and based on recommendations provided by the National Academy of Science (NAS) 2013 report entitled, *Assessing Risks to Endangered and Threatened species from Species* (<https://www.nap.edu/catalog/18344/assessing-risks-to-endangered-and-threatened-species-from-pesticides>). The interim methods are based on shared assumptions, data, analytical processes, and models with the understanding that the data and analyses used in EPA's biological evaluations will be used to inform the Services' biological opinions. The ultimate goal of this shared method is a streamlined consultation process that relies on best available data, data relevance, risk characterization, and robust quantitative and qualitative analyses.

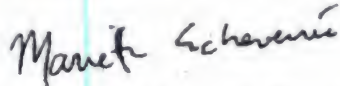
As specified in the agreed upon interim methods, data and analyses contained in the biological evaluations will be used, where possible, in the biological opinions for the three chemicals. The schedule for the Services to complete final nation-wide biological opinions for diazinon, chlorpyrifos, and malathion is December 31, 2017, pursuant to the stipulations filed in *Center for Biological Diversity (CBD) v. FWS (3:11-CV-5108-JSW)* for listed species and designated critical habitat under the jurisdiction of FWS, and *Northwest Center for Alternatives to Pesticides (NCAP) v. NMFS (CV-1791-RSL)* for listed species and designated critical habitat under the jurisdiction of NMFS.

The final biological evaluations for diazinon, chlorpyrifos, and malathion including all attachments, appendices, and provisional models used to complete the analysis are available at:

[<https://www.epa.gov/endangered-species/implementing-nas-report-recommendations-ecological-risk-assessment-endangered-and>].

We look forward to continued collaboration with the Services as well as the U.S. Department of Agriculture on further development of refined and improved techniques and approaches for nation-wide ESA Section 7 pesticide consultations. Please let me know if you have any questions regarding this request or the materials that have been collaboratively developed with the Services to initiate formal consultation.

Sincerely,



Marietta Echeverria, Director
Office of Pesticide Programs (7501P)

cc: Jack Housenger
Richard Keigwin
Yu-Ting Guilaran
Anita Pease
Mark Dyer
Gina Shultz
Cathy Tortorici
Sheryl Kunickis



United States Department of the Interior

FISH AND WILDLIFE SERVICE



NOV 14 2017


Marietta Echeverria
Director, Environmental Fate and Effects Division
Office of Pesticide Programs
Division Mail Code 7507P
U.S. Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, D.C. 20460

Dear Ms. Echeverria,

On January 18, 2017, the U.S. Fish and Wildlife Service (Service) received the Environmental Protection Agency's (EPA) draft Biological Evaluations (BEs) on the effects of reregistering chlorpyrifos, malathion, and diazinon under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and request to initiate formal consultation under section 7 of the Endangered Species Act of 1973, as amended (ESA). As you are aware, this effort was one of the most complex section 7 consultations ever attempted. While we appreciate the collaboration with the Service and others that informed the development of these BEs, after further review and lessons learned in consideration of the BEs the Service is requesting additional information necessary to complete formal consultation. (See interagency consultation regulations at 50 CFR §402.14). Specifically, we request:

- A revised effects analysis for each chemical that reflects the best scientific and commercial data that is currently available or which can be obtained during the consultation – the standard for information required under 50 CFR §402.14(d) for an action agency when seeking formal consultation – ~~regarding actual use, including extrapolation to areas where actual use data does not exist or cannot be obtained.~~ The revised effect analyses should also seek to predict effects from future usage that is reasonably certain to occur during the time period of the label authorization but is not reflected in current actual use data.
- A revised effects analysis for each chemical that eliminates from analysis geographic areas identified by EPA where these pesticides are not used and where such use is not likely during the time period of the label authorization, ~~or where listed species or designated critical habitats would not otherwise be exposed to use of the pesticide (e.g., certain states, high elevation areas, uninhabited islands).~~

In addition, the Service also suggests that the EPA monitor available use and usage information to determine if the manner of actual use remains consistent with assumptions of use and usage considered in the consultation process.

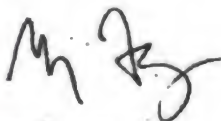
Under the regulations, indirect effects are "those that are caused by the proposed action and are later in time, but are reasonably certain to occur." 50 C.F.R. 402.02. The effects analysis determines the action area, which is "all areas to be affected directly or indirectly by the Federal action and not merely the immediate area involved in the action." 50 C.F.R. 402.02. We must keep in mind the ESA regulations when considering the action description and effects analysis. 

In the course of developing the draft and final biological opinions and associated incidental take statements, the Service requests that EPA facilitate coordination with the registrants and user groups to develop, if necessary, any reasonable and prudent alternatives to avoid violation of section 7(a)(2) of the Act and any reasonable and prudent measures necessary or appropriate to minimize the impact of your action on listed species.

This letter also serves as a request to extend the consultation, in accordance with 50 C.F.R. 402.14(e). Upon receipt of the above requested information, the Service will work with EPA to establish a schedule to complete consultation on the proposed actions.

If you have any questions or concerns about this request or the consultation process in general, please feel free to call me at 202-208-4646 or Deputy Assistant Director Gina Shultz at 703-358-1985.

Sincerely,



Gary Frazer
Assistant Director - Ecological Services



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

NOV 17 2017

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Mr. Gary Frazer
Assistant Director
U.S. Fish and Wildlife Service
Ecological Services
5275 Leesburg Pike
Falls Church, VA 22041-3803

Dear Mr. Frazer,

Thank you for your letter requesting additional information to complete formal consultation on the Biological Evaluations (BEs) for chlorpyrifos, malathion, and diazinon, which were finalized on January 18, 2017.

As you are aware, the BEs were developed with Services oversight and included all information and analyses as requested by the National Marine Fisheries Service (NMFS) and Fish and Wildlife Service (FWS) during their development. We understand, however, that in the course of our consultation, FWS has indicated that additional information regarding use and usage information could be of value in the development of the FWS biological opinions (BiOps). We will treat your letter as a request for additional information as described in section 402.14(f) of the FWS regulations and not a request to revise the EPA BEs with additional information under section 402.46(b). This is consistent with the regulations that require requests from FWS for additional information to be submitted within 45 days of EPA providing the BE to FWS (50 CFR Part 402). Accordingly, any agreement from EPA to supplement the consultation should not be viewed as EPA's agreement to either revise or withdraw its final BEs.

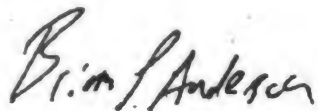
We are pleased that the utility of the use and usage information is being reconsidered, and we anticipate being able to provide this information within approximately 6 months.

Use information (e.g., maximum application rate, number of allowed applications, etc.) is extracted directly from product labels whereas usage information describes where, when, and how a pesticide is actually being used based on survey information. In order to provide the requested use and usage information, staff from EPA's Biological and Economic Analysis Division (BEAD) must compile and summarize label information, appropriately aggregate complex use directions, and develop associated usage statistics. The number of registered use sites for these active ingredients is extensive with more than 100 active registered products for

chlorpyrifos and diazinon. Additionally, this work would need to be completed concurrently with BEAD's existing workload to provide use and usage information supporting EPA's registration review program.

Your letter also requests to extend the consultation in accordance with 50 C.F.R.402.14(e). We agree that consultation should continue and be extended as necessary, and that any required consent from any applicants be obtained.

Sincerely,

A handwritten signature in black ink, appearing to read "Brian J. Anderson". The signature is written in a cursive, flowing style.

For Marietta Echeverria
Director, Environmental Fate and Effects Division
Office of Pesticide Programs



United States Department of the Interior

FISH AND WILDLIFE SERVICE
Washington, D.C. 20240



In Reply Refer To:
FWS/AES/DCHRS/039739

JAN 14 2009

Arthur-Jean B. Williams, Associate Director
Environmental Fate and Effects Division
Office of Pesticide Programs (7507P)
US Environmental Protection Agency
Washington, DC 20460

Re: Informal Consultation on the Effects of Diazinon and Racemic Metolachlor
Reregistration on the Endangered Barton Springs Salamander

Dear Ms. Williams,

This responds to the Environmental Protection Agency's (EPA) request for concurrence that the proposed reregistration of pesticides under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) containing the active ingredients diazinon and racemic metolachlor (metolachlor) are not likely to adversely affect the endangered Barton Springs salamander (*Eurocea sosorum*) pursuant to section 7 of the Endangered Species Act of 1973, as amended (ESA). The U.S. Fish and Wildlife Service (Service) received your request on May 16, 2007. EPA's assessments were based upon the process outlined in the January 2004 *Overview of the Ecological Risk Assessment Process in the Office of Pesticide Programs, U.S. Environmental Protection Agency*.

We have reviewed the information provided with your request, the relevant scientific and commercial literature available on the toxicity of diazinon and metolachlor, and the ecology of the listed species. We can not concur that the proposed action is not likely to adversely affect the Barton Springs salamander because a review of the information made available indicates that these pesticides may affect the Barton Springs salamander, yet the assessment did not address the full scope of the action, and subsequently, the full effects of the action. Specifically, EPA's assessment did not provide information on pesticide products and their constituents, environmental mixtures, worst-case scenario exposure estimates, temporal extrapolation for the full length of the action, or the full extent of data from the open literature.

Definition of the Proposed Action

Our two agencies, together with the National Marine Fisheries Service, discussed the proposed action of pesticide reregistration at the interagency meetings December 10-12, 2007. We collectively determined that the action is more complex than simply the reregistration of an active ingredient, and that it includes the authorization for the use or uses as described in labeling of pesticide products containing the active ingredient. EPA

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registers separately each pesticide product containing the active ingredients diazinon and metolachlor and approves the labels accompanying the products. Each label represents a legal document that describes the product formulation (including inert ingredients, additional active ingredients, and other adjuvants) and stipulates how and where a given pesticide may be used. Thus, the effects to listed species and their critical habitats from exposure to diazinon or metolachlor are the result of a suite of EPA actions: approvals of products containing the active ingredient diazinon and metolachlor, which includes the label instructions defining the legal use of those products.

It is our understanding that pesticide products containing diazinon and metolachlor are used widely throughout the United States and may affect numerous listed species and critical habitats. We further understand that EPA requests to build section 7 consultation compliance through a series of consultations, and that the requests for consultation on the Barton Springs salamander represent the first of many consultations on the effects of pesticide products containing diazinon and metolachlor.

Products containing more than one active ingredient and recommended tank mixes

We listed the products we are aware of that contain diazinon or metolachlor as an active ingredient in Attachment 1; however these lists may be incomplete or contain products that may have been cancelled. Some of these products may contain only diazinon or metolachlor as an active pesticide ingredient, while others contain one or more additional active pesticide ingredients as shown in Attachment 1. In addition, product labels frequently suggest tank mixes with other pesticide products for control of certain pest species.

While the relative effects of mixing pesticides are often unknown, there are some cases in which data exist to conclude that mixtures of active ingredients can have either an additive or synergistic effect. Such effects have been detected when either diazinon or metolachlor have been mixed with the pesticide atrazine. For example, atrazine has been shown to increase the toxicity of diazinon to the midge (*Chironomus tentans*) (Lydy 1997), and when combined with metolachlor, had a synergistic effect in retarding amphibian growth, resulting in potential ecological consequences to overwintering, fecundity, mate selection, food acquisition, and predator avoidance (Hayes 2006). Atrazine is one of the most widely used herbicides in the United States, and can be bought pre-packaged with metolachlor as a formulation or combined as the result of a recommended tank mix.

EPA's assessments lack sufficient information on the fate and effects of formulated mixtures of active ingredients or recommended tank mixtures for the Service to conclude that they are not likely to adversely affect the Barton Springs salamander. At a minimum, EPA should provide an evaluation of the effects of labeled ingredients separately, and discuss whether additive, synergistic, or antagonistic effects would be expected.

Inert Ingredients and/or Ingredients with Unknown Toxicity

EPA's assessments include comprehensive toxicity data for diazinon and metolachlor, but more limited data on whole-formulation toxicity. Of concern are the surfactants and unidentified proprietary inerts contained in products for which toxicity data is unknown to the Service. In order to properly assess the effects of the proposed action, the Service requests that EPA provide a list of inert ingredients present in diazinon- and metolachlor-containing products, and any known toxicity data for these chemicals. Service staff have been trained and authorized to handle propriety data that have been classified as Confidential Business Information and are prepared to do so, as appropriate.

Racemic metolachlor vs S-metolachlor

As outlined in your analysis, this consultation only applies to labels associated with the registration of racemic metolachlor (EPA pesticide code#108801). This product has been registered by EPA since 1976, and contains equal quantities of r- and s-enantiomers of metolachlor. In subsequent years, a separate registration was filed for S-metolachlor (EPA pesticide code#108800), whose formulation contains a higher percentage of the more biologically active s-enantiomer. Due to its enhanced efficacy as an herbicide, the use of S-metolachlor has surpassed that of racemic metolachlor in certain areas of the country. However, since the information you submitted with your request for consultation provides information and analyses only for racemic metolachlor, this consultation does not include the registration and use of products associated with the S-metolachlor registration as part of the proposed action. However, in order to accurately assess the effects of exposure to the chemical metolachlor to the Barton Springs salamander, total metolachlor concentrations monitored in the watershed will be considered, regardless of the source.

Exposure and Effects Assessment*Environmental Mixtures*

The effects of the action on a species or critical habitat can not be accurately characterized without first establishing the physical, chemical, and biological conditions in which the species occurs without the proposed action. By establishing the environmental conditions we can understand and explain what happens when chemicals in products containing diazinon or metolachlor are added to the chemicals in the waters supporting the Barton Springs salamander. The basis of comparison, under section 7, is environmental conditions without the proposed action (without approval of diazinon and metolachlor products) and environmental conditions with the proposed action (with approval of diazinon and metolachlor products). It is often the presence of an existing stressor that, when combined with a new stressor, triggers an adverse effect that otherwise may not occur. Alternatively, the new stressor may exacerbate existing adverse effects or possibly diminish the influence of existing stressors.

The list of existing chemical components in the water column should include, as appropriate, other pesticide products presently sold and used in the action area. Although EPA's approval of these pesticide products may not have undergone section 7 consultation, it is a fact they are presently available and are being used and many of them

will co-occur in the water column with diazinon and metolachlor at least until they have undergone FIFRA review and separate section 7 consultation.

For listed species and critical habitats that are wholly aquatic in nature, exposure to environmental mixtures can be characterized by assessing the chemical loads that occur in the water column regardless of their mode of transport (e.g., direct application or drift, overland runoff, and atmospheric or groundwater transport). In this way, we would capture the effects to listed species when exposed to mixtures of pesticides irrespective of whether the source was a mixture of ingredients in a formulated product, a tank mixture, or the application of separate pesticide products on adjacent areas within a watershed. Available data can be utilized to develop assumptions about exposure to other constituents in the water column focusing on those constituents for which diazinon or metolachlor are suspected of having additive, synergistic, or antagonistic effects.

In our December 10-12, 2007, interagency meetings, EPA asserted that its assessments were complete and represented the "best available scientific and commercial data," even though environmental mixtures were not factored into the analyses of effects of the action. At the December meeting the Service offered to develop this analysis as part of its first Biological Opinions with the expectation that EPA would incorporate consideration of environmental mixtures into future assessments and consultation requests.

Modeled Exposure Estimates

In the absence of monitoring programs designed to capture peak and chronic pesticide concentrations in the action area, EPA has developed models to estimate the range of pesticide concentrations to which species and critical habitats are likely to be exposed. However, when populating and interpreting data from these models, EPA selectively utilized input and output parameters designed to estimate "high-end" exposure concentrations and not reasonable worst-case scenarios. For example, EPA's high-end estimate is based on a 1-in-10-year peak concentration in waters surrounded by soils typical of the action area, but not may represent a peak for a longer time period on soil especially vulnerable to runoff. While concentrations of diazinon and metolachlor in samples previously collected from Barton Springs are not greater than the high-end estimates predicted by EPA in these assessments, pesticide concentrations measured from regions with more robust data sets have exceeded EPA's predicted peak concentrations in other assessments. Given these discrepancies, and that registration review of pesticides is based on a 15-year cycle, we do not believe the 1-in-10-year peak concentration estimate meets ESA's mandate to "insure" jeopardy is not likely.

If the worst-case exposure could reasonably be expected to adversely affect a listed species or critical habitat, then it would be useful to further characterize the range, frequency, and duration of various exposure concentrations in order to determine whether anticipated adverse effects would likely jeopardize listed species or adversely modify critical habitat.

Urbanization of the Action Area

In 2006, EPA initiated a registration review program to reevaluate all pesticide registrations on a 15 year cycle. Thus, the action considered in this consultation, authorization for uses as described in labeling of pesticide products containing diazinon or metolachlor, will remain in effect for a span of 15 years. This interval establishes the minimum time horizon that should be considered in EPA's assessments and effects determinations. While the assessments do an adequate job of describing current pesticide use in the Barton Springs area, they do not adequately estimate future pesticide use and transport. The action area is undergoing rapid suburban development (Texas State Data Center 2002) that could have implications for future pesticide use. Increasing subdivision development usually results in greater amounts of impervious surface on the landscape (Arnold and Gibbons 1996), which further increases the likelihood of pollutant transport into the Barton Springs portion of the Edwards aquifer (City of Austin 1990). Due to its limited use in the action area, the effect of this development on metolachlor use is anticipated to be small. For diazinon, the entire estimated environmental concentration (EEC) is based on its potential use on a single orchard and three nurseries with outdoor wholesale production. Though it is very difficult to predict whether additional ornamental nurseries will become established in the action area during the duration of the action, the development of even one new facility will significantly increase the potential diazinon use in the action area therefore increasing effects to the salamander given the potential for indirect effects via reduction of prey availability. Concentrations of diazinon exceeded levels of concern for acute risk to sensitive aquatic invertebrates on four separate occasions at Main Barton Spring from 2000 to 2005 and on two occasions at Upper Barton Spring during the same time period. The study by Sanchez et al. (1999) indicates that reproductive effects to daphnia can occur at concentrations orders of magnitude below both acute mortality rates and peak concentrations modeled for the springs. We recommend that impacts of the entire scope of the action be addressed by EPA.

Use of Data from the Open Literature

The assessments contain bibliographies of open literature references related to each pesticide that were derived from EPA's ECOTOX database of single chemical toxicity information for aquatic and terrestrial life. Amongst those references, EPA lists those accepted for inclusion in the ECOTOX, but not acceptable for use by the Office of Pesticide Programs (OPP) for use in endangered species risk assessment. Within these lists, the Service found several examples of studies that appear to contain information relevant to these effects determinations and that should be considered by EPA in this analysis (Attachment 2).

For diazinon, many of the references rejected by OPP pertained to sublethal endpoints related to histopathology or biochemical effects in taxa of concern for these analyses (ie., fish, invertebrates, and plants). For this assessment, the Service has reviewed these studies and determined that either no effect was found from pesticide exposure or that concentrations found to cause adverse effects are above those identified and utilized by EPA as low-effect levels. However, future assessments will not be considered as

complete without full review and incorporation of all relevant data into the effects analysis by EPA.

For metolachlor, one reference rejected for use by OPP (Vykusova and Svobodova 1987), reports a fish LC50 value of 20 ug/L – greater than expected EECs in the Barton Springs action area, yet lower than the LC50 used in this analysis. This paper was rejected by OPP because it was published in a foreign language. However, the ESA's standard of "best available information" does not exclude publications in foreign languages. As this paper provides information not available from another source and is relevant to establishing an effects threshold, EPA should provide a full evaluation of this study in further consultations, and incorporate this endpoint into its effects analysis where applicable.

If predicted peak or chronic EECs change with modifications to EPA's modeling, data from the open literature must be re-reviewed to determine if sublethal effects are expected to occur at these levels.

Recommendations

In order to complete section 7 consultation on the use of pesticides products containing diazinon and metolachlor and their effects on the Barton Springs salamander, we require the following information:

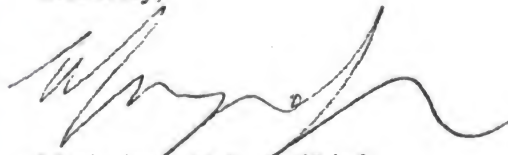
1. A list of all pesticide products registered by EPA that contain diazinon or metolachlor and could be used in the watershed supporting the Barton Springs salamander, a list of the chemical constituents contained in each product and any known toxicity data for the constituents, and the approved labels describing uses and limitations of uses of the products that could help estimate the potential effects to listed species and critical habitats.
2. An improved modeling approach that predicts a reasonable worst case scenario for the assessed action areas suitable for determining whether formal consultation is needed, and a more extensive analysis to support formal consultation, if necessary. We recommend developing the needed modeling collaboratively in order to prevent further delays in completing consultation.
3. An estimate of diazinon EECs given the projected increased urbanization of the action area over the next 15 years. The Texas State Data Center predicts a population increase in the Austin metropolitan area of up to 93% by 2030 ((Texas State Data Center 2002). To account for this potential growth, EPA should model a corresponding increase in impervious surfaces and assume a doubling in the number of nurseries with potential diazinon use. As the population trend is towards increased urbanization, it is acceptable to assume that diazinon use on orchards will not increase.

4. An estimate of existing and future pollutant loads in the Barton Springs waterway as a basis for determining whether the salamander is likely to be adversely affected by the addition of diazinon and metolachlor and, if so, an analysis of the extent of effects over the reregistration period. The Service and NOAA are developing methods for weighing the influence and effects of "environmental mixtures." EPA may choose to await development and use the Services approach or adopt their own methods for considering existing environmental conditions in effects analyses.

We recommend the continuation of informal consultation on the effects of diazinon and metolachlor on the Barton Springs salamander. We recommend implementing a strategy that builds section 7 compliance for the reregistration of pesticide products containing these active ingredients. We can begin building section 7 compliance by evaluating the effects of diazinon and metolachlor products on the Barton Springs salamander. Additional consultations will be necessary for other listed species and designated critical habitats that occur in the action area and may be affected by the approval of these products before EPA can meet the mandate to insure re-registration of the relevant pesticide products are not likely to jeopardize species or destroy or adversely modify critical habitats. Section 7 compliance for a particular product could be achieved when all of the relevant ingredients (e.g. all active ingredients, "inerts," etc.) have been evaluated for all of the listed species likely to be exposed to the use of that product.

We look forward to working together to achieve compliance with the Endangered Species Act on your FIFRA actions. If you have any questions about our comments or recommendations, please contact Dan Buford or Nancy Golden at (703) 358-2106 or via e-mail at Daniel_Buford@fws.gov or Nancy_Golden@fws.gov.

Sincerely,



Marjorie A. Nelson, Chief
Branch of Consultation & HCPs
Division of Consultation, Habitat
Conservation Planning, Recovery and
State Grants

Enclosures

Enclosure 1: Diazinon and Metolachlor Products Currently Labeled for Use in the U.S.
Data from this table were derived from www.cdms.net, and www.greenbook.net.

Manufacturer	Trade Name	Active Ingredients (%)		
Makhteshim Agan	Diazinon 50W	Diazinon 50%		
Helena	Diazinon AG500	Diazinon 48%		
Wilbur-Ellis	Diazinon 14G	Diazinon 14.3%		
UAP- Loveland Products	Diazinon AG600 WBC Insecticide	Diazinon 56%		
UAP- Loveland Products	Diazinon 5 Granules			
UAP- Loveland Products	Diazinon 50WP insecticide	Diazinon 56%		
UAP- Loveland Products	Diazinon AG500 Insecticide			
Drexel Chemical Company	Diazinon Insecticide			
Makhteshim Agan	Diazinon AG500	Diazinon 48%		
Helena	Kickstart	Diazinon 15%	Lindane 25%	Carboxin 14%
Drexel	Me Too Lachlor	Metolachlor 86.4%		
Drexel	Me Too Lachlor II	Metolachlor 84.4%		
Makhteshim Agan	Parallel	Metolachlor 84.4%		
Makhteshim Agan	Parallel PCS	Metolachlor 86.4%		
Makhteshim Agan	Parallel Plus	Metolachlor 28.9%	Atrazine 30%	Atrazine related 0.5%
Monsanto	Parrlay	Metolachlor 86.4%		
Drexel	Trizmet II	Metolachlor 26.1%	Atrazine 33.1%	Atrazine related 0.6%
Sipcam Agro USA, Inc.	Stalwart	Metolachlor 86.4%		
Sipcam Agro USA, Inc.	Stalwart C	Metolachlor 84.1%		
Sipcam Agro USA, Inc.	Stalwart Xtra	Metolachlor 26.1%	Atrazine 33%	Atrazine Related compounds 0.7%
Tenkoz, Inc.	Triangle	Metolachlor 34.5%	Atrazine 28.6%	Atrazine related compounds 0.5%

Enclosure 2 ECOTOX accepted references, not acceptable for OPP, that appear to contain information relevant to endangered species effects determinations

Diazinon:

Anees, M. A. (1978). Haematological Abnormalities in a Freshwater Teleost, *Channa punctatus* (Bloch), Exposed to Sublethal and Chronic Levels of Three Organophosphorus Ins. *Int.J.Ecol,Environ.Sci.* 4: 53-60.

EcoReference No.: 6960

Chemical of Concern: DMT,DZ,MP; Habitat: A; Effect Codes: BCM,CEL; Rejection Code: NO ENDPOINT(ALL CHEMS).

Anees, M. A. (1978). Hepatic Pathology in a Fresh-Water Teleost *Channa punctatus* (Bloch) Exposed to Sub-lethal and Chronic Levels of Three Organophosphorus Insecticides. *Bull.Environ.Contam.Toxicol.* 19: 524-527.

EcoReference No.: 6099

Chemical of Concern: DMT,DZ,MP; Habitat: A; Effect Codes: CEL; Rejection Code: NO ENDPOINT,CONTROL(ALL CHEMS).

Anees, M. A. (1976). Intestinal Pathology in a Freshwater Teleost, *Channa punctatus* (Bloch) Exposed to Sub-lethal and Chronic Levels of Three Organophosphorus Insecticides. *Acta Physiol.Latinoam.* 26: 63-67.

EcoReference No.: 6100

Chemical of Concern: DMT,DZ,MP; Habitat: A; Effect Codes: CEL; Rejection Code: NO ENDPOINT(ALL CHEMS).

Banu, N., Mustafa, G., Khan, A. M., and Ahmed, M. (1984). Histopathological Effects of Diazinon on the Gonads of Freshwater Catfish, *Heteropneustes fossilis* (Bloch). *Dhaka Univ.Stud.Part B* 32(1): 17-23.

EcoReference No.: 11577

Chemical of Concern: DZ; Habitat: A; Effect Codes: CEL; Rejection Code: NO ENDPOINT(DZ).

Butler, G. L., Deason, T. R., and O'Kelley, J. C. (1975). The Effect of Atrazine, 2,4-D, Methoxychlor, Carbaryl and Diazinon on the Growth of Planktonic Algae. *Br.Phycol.J.* 10: 371-376.

EcoReference No.: 7429

Chemical of Concern: 24DXY,ATZ,CBL,DZ; Habitat: A; Effect Codes: POP; Rejection Code: NO ENDPOINT(ALL CHEMS).

Chatterjee, K. and Konar, S. K. (1984). Effects of the Pesticide Diazinon at Various pH and Turbidity on Fish and Aquatic Ecosystem. *Aquat.Sci.Fish.Abstr.* 14(11, Pt.1):263 / *Environ.Ecol.* 2: 49-53.

EcoReference No.: 11693

Chemical of Concern: DZ; Habitat: A; Effect Codes: GRO; Rejection Code: NO
ABSTRACT.

Conners, D. E. and Black, M. C. (2004). Evaluation of Lethality and Genotoxicity in the Freshwater Mussel *Utterbackia imbecillis* (Bivalvia: Unionidae) Exposed Singly and in Combination to Chemicals Used in Lawn Care. *Arch.Environ.Contam.Toxicol.* 46: 362-371.

EcoReference No.: 74236

Chemical of Concern: ATZ,GYP,DZ,CBL; Habitat: A; Effect Codes: MOR; Rejection Code: LITE EVAL CODED(ATZ,CuS),OK(ALL CHEMS).

Doggett, S. M. and Rhodes, R. G. (1991). Effects of Diazinon Formulation on Unialgal Growth Rates and Phytoplankton Diversity. *Bull.Environ.Contam.Toxicol.* 47: 36-42.

EcoReference No.: 10596

Chemical of Concern: DZ; Habitat: A; Effect Codes: POP; Rejection Code: NO
ENDPOINT(DZ).

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Chemical of Concern: PPB,DZ; Habitat: A; Effect Codes: BCM,ACC,MOR; Rejection Code: NO MIXTURE (PPB).

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Chemical of Concern: CBL,DZ,MLN; Habitat: A; Effect Codes: PHY,POP; Rejection Code: OK(CBL,MLN),NO ENDPOINT(DZ).

Reyes, J. G. G., Dalla-Venezia, L., and Alvarez, M. G. L. (2002). Effect of Some Organophosphorus Pesticides on Oxygen Consumption of Shrimp, *Litopenaeus vannamei*. *Ecotoxicol. Environ. Saf.* 52: 134-136.

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Chemical of Concern: DZ, AZ; Habitat: A; Effect Codes: PHY; Rejection Code: NO ENDPOINT(ALL CHEMS).

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Diazinon DRAFT/REFs 1999//

EcoReference No.: 8259

User Define 2: ECOTOX MED, WASH, CALF

Chemical of Concern: CBF, DZ

Endpoint: BEH, PHY; Habitat: A; Rejection Code: NO ENDPOINT.

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Chemical of Concern: DZ; Habitat: A; Effect Codes: CEL; Rejection Code: NO ENDPOINT(DZ).

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EcoReference No.: 312

User Define 2: ECOTOX MED, WASH, CALF

User Define 3: 05/27/04

Chemical of Concern: ATZ, MTL

Endpoint: MOR; Habitat: A; Rejection Code: NO FOREIGN.

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COMMITTEE QUESTIONS FOR AGENCY AND SERVICES

QUESTIONS FOR EACH AGENCY TO ADDRESS – EPA, NMFS, FWS

1. For each topic in the committee's statement of task, list no more than three defining elements that differentiate your agency's approach from that of the other agencies. Illustrate with examples.

a. Best available scientific data and information.

The Service's protocol for obtaining the best scientific and commercial information to inform the Biological Opinion is described in the Interagency Cooperative Policy on Information Standards Under the Endangered Species Act (FR, July 1, 1994 (Vol. 59), p. 34271)

The policy states that:

The Services receive and use information on the biology, ecology, distribution, abundance, status, and trends of species from a wide variety of sources as part of their responsibility to implement the Act. Some of this information is anecdotal, some of it is oral, and some of it is found in written documents. These documents include status surveys, biological assessments, and other unpublished material (that is, "gray literature") from State natural resource agencies and natural heritage programs, Tribal governments, other Federal agencies, consulting firms, contractors, and individuals associated with professional organizations and higher educational institutions. The Services also use published articles from juried professional journals. The reliability of the information contained in these sources can be as variable as the sources themselves. As part of their routine activities Service biologists are required to gather, review, and evaluate information from these sources prior to undertaking listing, recovery, consultation, and permitting actions.

To assure the quality of the biological, ecological, and other information that is used by the Services in their implementation of the Act, it is the policy of the Services:

a. To require biologists to evaluate all scientific and other information that will be used... (e) to prepare biological opinions, incidental take statements, and biological assessments... This review will be conducted to ensure that any information used by the Services to implement the Act is reliable, credible, and represents the best scientific and commercial data available.

d. To the extent consistent with sections 4, 7, and 10 of the ESA, and to the extent consistent with the use of best scientific and commercial data available, use primary and original sources of information as the basis for recommendations to (6) make determinations of whether a Federal Action is likely to jeopardize a proposed, threatened, or endangered species or destroy or adversely modify critical habitat...

The policy is inclusive, acknowledging that relevant information may take different forms and come from a variety sources, and relies on the best professional judgment of Service. Information quality is evaluated in much the same way as scientific manuscripts are reviewed for publication. We review the experimental design, methodologies, reporting of results and

whether the conclusions are supported by the data in order to determine whether the information is reliable and credible.

EPA's protocol imposes limitations which may exclude relevant data of acceptable quality that would otherwise inform the consultation. Some examples of the type of data/studies that are either excluded or not considered in EPA's risk analysis: toxicity data derived from non-native species; papers published in a foreign language journal, field studies, and sublethal effects data that are not quantitatively linked to higher order/apical responses.

For example, in our analysis of EPA's effects determination for the effects of metolachlor and diazinon on the Barton Springs salamander (USFWS 2009a), FWS identified examples of studies that appeared to contain information relevant to these effects determinations and that should be considered by EPA in this analysis. For diazinon, many of the references rejected by EPA pertained to sublethal endpoints related to histopathology or biochemical effects in taxa directly related to the analysis (i.e., fish, invertebrates, and plants). For metolachlor, one reference rejected for use by EPA reported a fish LC50 value that was lower than the LC50 used in the analysis. This paper was rejected because it was published in a foreign language. The ESA's standard of "best available information" does not exclude publications in foreign languages. When a data source provides information and is relevant to determining the effects of the action upon listed species – in this case establishing an effects threshold – we are bound to conduct a full evaluation of the information and incorporate the endpoint into its effects analysis where applicable, regardless of the original language of publication.

We remark on further aspects of capturing and utilizing the best available data in questions 4, 5, and 9.

b. Sub-lethal, indirect, and cumulative effects

Sublethal effects

In the context of Section 7 consultations, sublethal effects which "may affect" an individual by modifying physiological functions or behavior in an adverse way must be evaluated for their potential to affect the species, its populations, or its individuals. Sublethal effects are taken into account as the Service develops risk hypotheses based on toxicant-specific assessment endpoints. By design, the Service's approach casts a wide net for each potentially affected species to ensure that the most sensitive endpoints are captured and evaluated, and that the most vulnerable life stages, life histories, and habitats are addressed. The process is intended to avoid overlooking potential adverse effects to listed species.

The category of sublethal effects includes data describing responses to pesticide exposure that are not quantified in terms of EPA's traditional endpoints of survival, growth, or reproduction. Any response that does not fit into one of these three categories is labeled "sub-lethal" whether or not the response would be expected to affect individual fitness, including survival. Such data may describe effects such as reductions in olfactory performance, endocrine disruption, or histological studies of organ tissue damage. At present, data describing "sub-lethal" effects are acknowledged but then set aside and not used by EPA in making effects determinations or characterizing the potential effects of the action, unless other data or studies are available that

would enable EPA to quantify a relationship between the "sub-lethal" effect and EPA's traditional endpoints, survival, growth, or reproduction.

(b) (5)

[listed species] (i.e., survival, growth, and reproduction of individuals)." For the Alabama sturgeon, EPA substantiated this conclusion by noting that "effects to reproduction, growth, and survival were not observed in the four submitted fish life-cycle studies at levels that produced the reported sublethal effects." We find error in this reasoning in that full life-cycle studies are not designed to capture the end result of many relevant sublethal effects to these endpoints.

While life-cycle tests evaluate chronic effects of pesticides over a full generation, they do so under conditions designed to rule out the effects of all other stressors: accessible food, proximity of mates, lack of predators, absence of migration, etc. These important ecological parameters (finding a mate, feeding, escaping predation, migrating, etc) are important endpoints that may be affected by sublethal effects such as decreased olfactory ability, altered schooling behavior, etc., that have direct consequences for survival and reproduction. These parameters are simply not measured in a full life cycle test. When appropriately tested in mesocosms that incorporate other

stressors, several studies have documented that sublethal responses from pesticide exposure result in adverse effects to individuals challenged by factors such as predation, interspecific competition, and disease state (reviewed by Grue et al., 1997 and Reylea and Hoverman 2006).

In our nonconcurrence letter to EPA on their analysis of the effects of atrazine to the Alabama sturgeon and dwarf wedgemussel (USFWS 2008), we identify several studies showing sublethal effects to fish and mussels at concentrations below the peak EECs identified for these species. The FWS concluded that these sublethal endpoints have direct bearing on the survival, growth, and reproduction of individuals. For example, morphological alterations to the renal system were found to occur in rainbow trout (*Oncorhynchus mykiss*) experimentally exposed to atrazine concentrations below EECs modeled for Alabama sturgeon habitat. While EPA did not incorporate this information in their analysis, we considered the physiology of the species to extrapolate potential effects to its fitness. Specific renal histological changes described included a proliferation of podocytes that almost completely occluded the area of filtration inside Bowman's capsule, a thickening of the glomerular basement membrane in the renal corpuscle, and mitochondrial myopathy in renal tubules. For freshwater fish, the constant inflow of water into the body must be properly regulated to avoid osmotic water loading and salt depletion. Glomerular filtration in the kidney functions as a major contributor to osmoregulation by delivering large volumes of extracellular fluid to the urinary space for excretion, while filtered salts are reabsorbed without water. Alterations to these filtering processes could affect both water and electrolyte balance in the organism. We consider these effects to have bearing in the fitness of individuals.

Similarly, atrazine effects to olfaction in fish were described in the open literature at concentrations below EECs, but not utilized by EPA in making its effects determination. While no data were specifically available that quantitatively linked these effects to survival or reproduction, we examined the role of olfaction in sturgeon of the Acipenseridae family and found that olfaction is an integral factor in many processes that affect individual fitness. While olfaction is fundamental to feeding, mating, homing, and predator avoidance behaviors in most fish, sturgeon, which have poorly developed vision, are generally even more reliant on olfactory performance than other taxa. Unlike most fish species that rely on vision for food searching behavior, sturgeon are unable to orient, make distant or near searches for food, or discover approaching objects based on visual cues and must rely on the olfactory system as the primary sensory system for feeding. For reproductive behavior, the involvement of chemical signalization in both finding a partner for spawning and determining their readiness is well studied and universal for all fish. Studies examining sturgeon specifically have documented male reactions to female sexual pheromones that suggest that males use olfaction to detect ripe females at spawning sites. We extrapolate this information on sturgeon physiology and life history to make linkages between the toxic effects of atrazine to olfaction and the potential effects to Alabama sturgeon exposure to this pesticide.

Indirect Effects

"Indirect effects" are defined by regulation (see 50 CFR 402.02) as those effects that "are caused by the proposed action and are later in time, but still are reasonably certain to occur." Such effects may occur outside of the area where a pesticide is applied. As we stated in our "Hazen

letter” to EPA, indirect effects may be difficult to identify and assess, given limited available data and causal relationships that are not always understood.

EPA acknowledges pesticides have the potential to cause indirect effects to listed organisms, for example, affecting prey availability and habitat suitability. EPA’s approach only considers potential direct effects to those resources immediately relevant to the listed species and would systematically miss potential tertiary effects or relevant community-level effects (e.g., reduction in prey availability because of toxicity to the prey’s foraging base or changes in community structure that favor competitors).

In assessing the potential for indirect effects EPA lists, a-priori, the taxonomic groups that comprise the primary prey and habitat-related taxa relevant to the listed species’ life history. These taxonomic groups are listed in the Overview Document as:

- birds (mallard duck and bobwhite quail) used as a surrogate for terrestrial-phase amphibians and reptiles;
- mammals (laboratory rat);
- freshwater fish (bluegill, sunfish, rainbow trout, and fathead minnow) used as a surrogate for aquatic-phase amphibians;
- freshwater invertebrates (*Daphnia magna*);
- estuarine/marine fish (sheepshead minnow);
- estuarine/marine invertebrates (*Crassostrea virginica* and *Mysidopsis bahia*);
- terrestrial plants (corn, soybean, carrot (radish or sugar beet), oat (wheat or ryegrass), tomato, onion, cabbage (cauliflower or Brussels sprout), lettuce, cucumber); and,
- Algae and aquatic plants.

These broad taxonomic groupings represent all species to be considered in an evaluation.

EPA uses the direct effects LOCs for these taxonomic groups to infer whether the listed species would likely be indirectly affected. For example, if a taxonomic group representing the listed species’ prey or habitat were directly affected, EPA infers the listed species would likely be indirectly affected. Potentially important “tertiary” effects and community-level effects are not considered. By making decisions a priori, an analysis may not consider more complex and realistic ecological interactions created by the addition of the pesticide, such as keystone effects, resource competition, predator-prey effects, multi-trophic level effects, density-mediated effects, or mutualism (Rohr et al. 2006). While these effects cannot be elucidated through conventional single-pesticide/single-species toxicity tests, many of these ecological interactions have been demonstrated in mesocosm studies that study the effects of pesticides in more realistic community structures (e.g., Boone and James 2003, Boone et al. 2004, Rohr and Crumrine 2005). In crafting a biological opinion, the FWS would look at all of the effects to the environment from the action, and assess the logical pathways that may lead to effects to listed species, based on our knowledge of community structure, life history characteristics, etc.

Cumulative Effects

The FWS does not have concerns with how EPA characterizes “cumulative effects.” Cumulative effects are characterized in a section separate from the “Effects of the Action” and are defined by

regulation as, "those effects of future State or private activities, not involving Federal activities that are reasonably certain to occur within the action area of the Federal action subject to consultation."

"Cumulative effects" are often misinterpreted as meaning the "aggregate" effects of an action on the individuals, populations, and status of a listed species or critical habitat. The open literature may describe a range of responses to exposure of a pesticide product. If only the most sensitive response, or "endpoint," is considered and not the aggregate of the responses to the effects of the action on an individual's fitness, then the analysis may not adequately characterize the manner in which the action may affect a listed species.

c. Mixtures and Inert ingredients

Mixtures

Mixtures are part of the existing conditions influencing the status of listed species. In our assessment of EPA's registration of pesticides, we consider the occurrence of mixtures as a result of formulated products, labeled recommended tank mixes, and environmental mixtures. As we describe below, exposure of organisms to pesticide mixtures is the norm rather than the exception.

Inert Ingredients

In 2007, the Services and EPA collectively determined that the proposed action for a pesticide registration is more complex than simply the registration of an active ingredient, but the authorization for its use or uses as described in labeling of pesticide products containing that active ingredient. EPA registers separately each pesticide product containing a particular active ingredient and approves the labels accompanying the products. Each label represents a legal document that describes the product formulation and how it is authorized to be used. Our consultation is on the approval of these labels. Almost all pesticide products are mixtures of one or more active ingredients combined with so-called "inert" ingredients. An active ingredient is one that prevents, destroys, repels, or mitigates a pest. Inert ingredients are simply those ingredients within the pesticide formulation that are not active ingredients. Inert ingredients are often included in a formulation to enhance the efficacy of the product but may have toxic effects. Currently, disclosure of inert ingredients on the product label is not required, and the exact formulation of a pesticide product may be considered proprietary information.

Nearly 4,000 inert ingredients have been approved by EPA for inclusion in pesticide products (USEPA 2011a). Only chemicals appearing on this list can be a constituent of a formulated product. It is the norm for pesticide products to contain some percentage of other ingredients in addition to the active ingredient(s). For example, in our assessment of 64 products in our nonconcurrence letter for atrazine (USFWS 2008), the percent of atrazine (or in combination with other active ingredients) varied greatly, ranging from 1.05% to 91%. No product was comprised solely of atrazine. For diazinon, no product contained greater than 56% of diazinon or other other active ingredients combined, and for metolachlor, percentages ranged from 60 to 84% (USFWS 2009). The presence of inert ingredients presents challenges on two levels: for some products the inert ingredients in the product are simply unknown and for others, the ingredients are known, but the data available to assess effects to listed species is either absent or insufficient. It is unclear how data were assessed to achieve the current set of approved inerts.

Toxicity data for these ingredients ranges from well-characterized to nonexistent. At the extreme, there are a number of inerts for which EPA can provide no toxicity data, nor can estimates of acute toxicity be calculated because the structure of the compound is unknown. Unlike active ingredients, inert ingredients do not have a "required" data set; however, EPA stipulates that it must have sufficient data to make a safety determination regarding human health and the environment. In its guidance documents, EPA lists types of data used to make approval decisions for new inert ingredients, but does not outline specific types of studies required or minimum data sets needed for approval (USEPA 2010).

While the evaluation of the effects of pesticide products to non-target organisms often relies on toxicity data for active ingredients, pesticide formulations can better be described as mixtures of two or more chemicals. The toxicity of inert ingredients, both alone and in conjunction with other chemicals in a pesticide formulation, is of considerable interest to the FWS. Several scientific studies have documented cases where inert ingredients caused an adverse effect in test organisms that was either absent or less severe when tested with the active ingredient alone. Koyama et al. (1997) determined that an herbicidal formulation of glufosinate caused a decrease in blood pressure and changes in heart rate of rats, *in vivo*. Glufosinate alone had no effects on either parameter. Another study by Peixoto, 2005, determined that the active ingredient in Roundup, glyphosate, had no relevant effect on mitochondrial bioenergetics of rat liver cells while the glyphosate formulation produced measureable toxicity. Another example of adverse effects by specific inert ingredients to fish is the study by Arsenault et al. (2004) which reported that exposure of salmon to environmentally relevant levels of the inert surfactant 4-nonylphynol resulted in reduced growth of the smolts. And in many cases formulated products have been found to have higher toxicity to non-target organisms than active ingredients alone and include juvenile mussels exposed to atrazine products (Bringolf et al. 2007a), juvenile and glochidial mussels exposed to glyphosate products (Bringolf et al 2007b), and chicks exposed to 2-4 D products (Arias 2003). EPA produced a Registration Eligibility Decision (RED) for Glyphosate in 1993 that documented the fact that some formulations of glyphosate are 10-100 times more acutely toxic to fish than is the active ingredient alone.

EPA's assessment of inert ingredients is generally limited to situations where data exist on the acute toxicity of a formulated product, using the rat as a test species. It is noteworthy that in none of the examples above would this analysis likely have elucidated the adverse effects revealed by these investigations. The assumption that acute testing of the formulated product will adequately reveal adverse effects of inert ingredients supposes that the inert ingredients will possess either a similar mode of action that enhances the acute toxicity of the active ingredient or otherwise potentiates its effect. We agree with EPA that in most cases the active ingredient is likely to be the most acutely toxic element of a formulation. However, we have inadequate data to conclude the other ingredients in the formulation will not elicit chronic or sublethal effects of a dissimilar nature, such as those put forward as examples above. The Service does not feel that extrapolation from acute mammalian testing is adequate to assess risk across taxonomic groups, nor from chemicals that are more likely to elicit sublethal or chronic low-level effects,

Multiple active ingredients: formulated products and recommended tank mixes:

Certain combinations of active ingredients have been pre-tested and known to be effective in the control of particular pests. These active ingredients may be pre-mixed and sold by the manufacturer as formulated product. In our analyses of EPA's submitted effects determinations, we have found that formulated products containing two or more active ingredients are not uncommon. For example, in our nonconcurrence letter to EPA on the effects of atrazine to the Alabama sturgeon and dwarf wedgemussel (USFWS 2008), we identified 64 products that contained the active ingredient atrazine. Of those 64 products, 55 were pre-formulated with one or more other active ingredient. In our nonconcurrence letter regarding the effects of metolachlor and diazinon to the Barton Springs salamander, we identify 1 of 10 diazinon products to contain multiple active ingredients, and 4 of 11 metolachlor products (USFWS 2009).

Other combinations of pesticides may be listed on the label as "recommended tank mixes." As we understand it, the mixture of pesticides is not regulated unless specifically prohibited on the label. This effectively means that any pesticide can be mixed with any other pesticide and applied concurrently. The recommendation of tank mixes on the product label is common, and a single label may recommend numerous other products. While the recommendation of tank mixes on the label does not preclude other mixes from occurring, it does make those labeled tank mixes a part of the federal action under consultation and requires EPA to insure that the use of the pesticide, as described in its labeling, will not jeopardize species.

Occurrence of mixtures in the environment

According to a large scale analysis of pesticide occurrence performed by USGS, more than 90% of the time water sampled from streams with agricultural, urban, or mixed land use watersheds contained 2 or more pesticides and degradates (of those sampled), and about 20% of the time they had 10 or more (Gillom et al. 2006). While we currently do not know of a means to identify every combination of pesticides that occurs within the habitat of listed species, the information in this report serves both to illustrate that environmental pesticides are the norm rather than the exception, and to identify pesticides that commonly co-occur together. This data may help to characterize the environment where data is lacking. The FWS seeks the committee's input on other methods to characterize environmental mixtures.

Analysis of pesticide mixtures

At present, EPA summarizes data available in the open literature regarding the effects of pesticide mixtures, and includes that summary as an appendix that is transmitted to FWS with its effect determination. These data are neither used to screen in species that might be affected by the action under consultation, nor to characterize potential effects to species that have already been determined to be likely to adversely affect listed species. The FWS feels that data may be suitable for making inferences about potential additive and synergistic effects to the aquatic species considered in this assessment.

While the relative effects of mixing multiple active ingredients are often unknown, there are some cases in which data exist to conclude that active ingredients can have either an additive or synergistic effect. Atrazine, for example, is a member of the chlorinated triazine group, which also includes the active ingredients simazine and propazine, and the chlorinated degradates desethyl-s-atrazine, desisopropyl-s-atrazine, and diaminochlorotriazine. Triazines are often mixed together into formulated products. These chemicals share a common mode of chemical

action and toxicity. As detailed in EPA's effects determinations for this compound, these active ingredients were consistently found to exhibit additive effects upon animals exposed concurrently. For human health, EPA routinely performs risk assessment concerning the cumulative effects from exposure to multiple chemicals that have a common mechanism of toxicity when making decisions related to pesticide tolerances, as required by the Food Quality Protection Act of 1996. For its human health risk assessment of atrazine, EPA concluded that the triazine pesticides and their metabolites should be included in a common mechanism group and considered through a cumulative risk assessment. This designation was based on a common neuroendocrine mechanism of toxicity which results in both developmental and reproductive effects. EPA has also performed cumulative assessments for organophosphates, carbamates, chloroacetanilides, and pyrethrins/pyrethroids. However, despite receiving effects determinations from EPA for many pesticides within these chemical classes, there have been no cumulative risk assessments performed for listed species.

Data may also exist for mixtures of active ingredients possessing dissimilar modes of action. Atrazine has been found to produce synergistic effects in organisms exposed concurrently with the herbicides metolachlor and alachlor. We know that these pesticides can be bought together as a pre-packaged formulated product, combined at the point of use as the result of labeled recommended tank mixes, and occur together in the environment. Gillom et al. (2006) found that atrazine and metolachlor were detected together in 77% of agricultural streams and 55% of urban streams. The combination of atrazine with metolachlor was found to have a synergistic effect in retarding amphibian growth, resulting in potential ecological consequences to overwintering, fecundity, mate selection, food acquisition, and predator avoidance (Hayes 2006). When atrazine was combined with the pesticide alachlor in a 50:50 mixture, 96-hour LC50's for rainbow trout (*Oncorhynchus mykiss*) and two amphibian species (*Rana pipiens* and *Bufo americanus*) were significantly lower than would be additively predicted (Howe et al., 1998). This data was included in initiation packages for each of these pesticides, but did not play a role in either the screening level risk assessment, or the full characterization of effects upon individual listed species. Underestimation of effects at the screening level could result in no further ESA-relevant effects analysis being done.

We believe that for listed species and critical habitats that are wholly aquatic in nature, exposure to environmental mixtures may be best characterized at this time by assessment of the chemical loads that occur in the water column regardless of their mode of transport (e.g., direct application or drift, overland runoff, and atmospheric or groundwater transport). In this way, we would capture the effects to listed species when exposed to mixtures of pesticides irrespective of whether the source was a mixture of ingredients in a formulated product, a tank mixture, or the application of separate pesticide products on adjacent areas within a watershed. Available data can be utilized to develop assumptions about exposure to other constituents in the water column focusing on those constituents for which a pesticide is suspected of having additive, synergistic, or antagonistic effects.

d. Models

In the absence of monitoring programs designed to capture peak and chronic pesticide concentrations in the action area, EPA has developed models to estimate the range of active ingredient concentrations to which species and critical habitats are likely to be exposed. These models are intended to estimate the worst-case exposure likely to occur as a result of the proposed action to enable EPA and the FWS to determine whether listed species or designated critical habitats were likely to be adversely affected. If the worst-case exposure could reasonably be expected to adversely affect a listed species or critical habitat, then it would be useful to further characterize the range, frequency, and duration of various exposure concentrations in order to determine whether anticipated adverse effects would likely jeopardize listed species or adversely modify critical habitat.

The Service is concerned that EPA's modeling efforts are not likely to estimate reasonable worst case exposure concentrations. The modeling often begins with conservative assumptions, but the additional modeling conducted and the values selected for variable inputs reduce or remove the conservatisms built into the modeling effort. When screening level estimates of exposure exceeded Levels of Concern (LOCs) based on GENECC2 modeling, EPA used the PRZM/EXAMS models previously reviewed by the Service to refine estimated exposure concentrations (EECs) based on site-specific conditions. However, rather than developing EECs based on model inputs specific to the action area, the EECs EPA reported were based on inputs developed for other geographic areas that may not be representative of the action area. For example, in our review of EPA's assessment of the effects of atrazine to the Alabama sturgeon and dwarf wedgemussel (USFWS 2008), EECs representing atrazine use on corn in the Chesapeake Bay and Alabama River watershed were estimated based on physiographic variables from Pennsylvania, sorghum from Kansas, and forestry from Oregon. These scenarios were expected to output high-end concentrations of atrazine in the action area based on soil and slope input parameters for generating runoff. However, examples from monitoring data in the Chesapeake Bay show that peak concentrations may be greater than those generated by modeling. For example, stream monitoring at areas of intense agricultural activity in the Choptank River watershed of Chesapeake Bay detected atrazine concentrations as high as 98 ug/L in a small stream, significantly higher than the peak EEC of 55 ug/L predicted using PRZM/EXAMS modeling. Using similar inputs, EPA also assessed the effects of atrazine to listed freshwater mussels, which spanned from Alabama north through the Midwest (USEPA 2007a). In this case, peak values from recent monitoring data were more than twice as high (209 ug/L) than peak screening-level EECs output by PRZM/EXAMS (84.5 ug/L) from the same region of the action area. Furthermore, EPA uses 1-in-10-year peak concentrations in waters surrounded by soils typical of the action area as high-end estimates. These estimates may not represent a peak in soil especially vulnerable to runoff, nor be representative of the time period of the action under consultation (15 years).

EPA's exposure assessments using these models are designed to be screening level assessments that should impart near 100% certainty that there is no risk. Screening level analyses should be conservative assessments that provide high levels of confidence in determining a low probability of adverse risk, incorporating uncertainty in a precautionary manner. Underestimation of effects at the screening level stage could result in no further ESA-relevant effects analysis being done. The FWS agrees that many of the input parameters into these models are highly conservative (e.g., assumption of all fields being sprayed simultaneous at maximum rates). As such, we

would expect the EECs to exceed any recorded monitoring data available, and not designed to capture peaks of pesticide use and runoff. Given exam we must assume that other parameters lack this conservatism. Because the considered to be screening level, even few data points that exceed modeled re-evaluate model input parameters. In fact, EPA's Overview Document st monitoring data shows higher detections than estimated by modeling, mode to be re-evaluated. In addition, due to the dearth of monitoring data for mo pesticides, we believe that when problems such as estimating pesticide conc detected for a data-rich pesticide such as atrazine, a reanalysis should be particular pesticide, but should extend to EPA's analysis of pesticide never have the luxury of field data for which to verify nor refute so modeling.

e. Interpretation of Uncertainty

A fundamental point of departure between the FWS and EPA lies in placed on having strong evidence that that an effect is likely to occur included in the assessment. Approaches that minimize "type I error (that an effect exists) typically come at the expense of increasing "type II error (concluding that no effect exists) and reliance on data with unknown does not provide strong support for the substantive requirement to a modification. In 1995, the National Research Council spoke extensively decisions under the ESA in the face of uncertainty (NRC 1995). In that as scientists, we are trained to minimize Type I error. However, choice may be appropriate for advancing scientific knowledge, it may when making management decisions. Instead, they advise to examine making each type of error. One of the consequences they identify is when related to endangered species, is the under-protection and per When uncertainties exist, the FWS relies upon the guidance to protect the species. (A more detailed discussion of this guidance is provided

Major sources of uncertainty in pesticide-related consultations include species and information regarding toxicity of pesticides. When there is data or uncertainty due to significant data gaps, the Service works to would work to the detriment of listed species (see NRC 1995; pg 14). toxicity of newly registered pesticides to listed species, FIFRA-required studies may provide us with data from as few as six surrogate species to estimate effects to over 1300 listed species. For long-registered pesticides, studies from the open literature may address some data gaps, but we are generally left with great uncertainty as we apply data across taxonomic groups and ecological guilds.

Some of the sources of uncertainty associated with estimating the risks of pesticides to listed species have been addressed through the use of uncertainty factors. For example, EPA develops levels of concern (LOC) by applying a factor to the acute measurement endpoint (the LC₅₀ for the most sensitive surrogate) to estimate a concentration that has negligible effects. For aquatic listed species this factor is 0.05 and for terrestrial listed species the factor is 0.1. This can be

interpreted as pesticide exposures that are less than or equal to one twentieth of the LC_{50} will have negligible effects on aquatic listed species. While EPA has incorporated a factor to adjust for measurement endpoint extrapolation, they have not accounted for uncertainty resulting from interspecies/inter-taxa variability in sensitivity. Because a relatively small number of species are tested compared to the large number of species they represent it is not likely that the surrogate species represents the most sensitive species within the taxa. For example, EPA estimated that "if two bird species are randomly tested and there are 650 species of birds in the United States, the probability of capturing an endpoint representing the most sensitive species is 2/650 or roughly 0.3 percent". We believe that some means of accounting for interspecies variability should be incorporated into the acute LOC or the effects assessment overall so that risk estimates are appropriate for all listed species within a taxonomic group.

For chronic exposures the measurement endpoint is the NOEC (for the most sensitive surrogate species) with a safety factor of 1. In other words chronic pesticide exposures that are less than or equal to the NOEC are expected to have negligible effects to listed species. However, we have little confidence that the NOEC consistently represents the true "no effect concentration" (see our response to question 5 paragraphs 3-5 for a more detailed explanation of our concerns regarding use of NOECs and LOECs) and therefore do not believe that the chronic LOC is a reliable metric for assessing risk. We also believe that some means of accounting for interspecies variability should be incorporated into the chronic LOC or the effects assessment overall so that chronic risk estimates are appropriate for all listed species within a taxonomic group.

Uncertainties associated with the potential effects from concurrent exposure of listed species to the active ingredient and other ingredients in the application product (i.e. adjuvants and additives, inerts, and other active ingredients) have been addressed in response to question 4. Whether those sources of uncertainty should/could be accounted for using uncertainty factors will depend on quantity and quality of available data, the reliability of the metric, and whether the OPP and the Services would have confidence in its use.

f. Geospatial Information and Datasets

In determining how and where pesticides are used, the agencies are considering the use of several datasets that provide insight into current practices. The agencies have agreed that the timeframe of consultation is 15 years, the length of time until a pesticide is to undergo registration review. The prediction of pesticide use over that timeframe based on data describing current use is challenging on several fronts.

- *Changes in crop patterns:* The demand for specific crops may change unexpectedly over that period of time, based on unforeseen factors. For example, the combination of rising gasoline prices and new bioenergy policies resulted in an increased demand for corn for ethanol production. Between the years 2000 and 2009, the harvested corn acreage increased by approximately 7.2 million acres, much of the change occurring rapidly over a 3-year period from 2006-2008 (USDA 2011). The change in the crop patterns was complex, including increasing acreage and shifting of crops grown.
- *Expansion of urban and residential areas:* For pesticides with residential uses, future use patterns may not be accurately represented by current use in areas experiencing

population expansion. For example, in our nonconcurrency letter for metolachlor and diazinon effects to the Barton Spring Salamander (FWS 2009), we determined that EPA's assessments do an adequate job of describing current pesticide use, but they do not account for the rapid suburban development in the action area. Increasing subdivision development usually results in greater amounts of impervious surface on the landscape, which further increases the likelihood of pollutant transport into the Barton Springs portion of the Edwards aquifer.

- *Infiltration or expansion of novel pest species:* Pesticide use must respond primarily to the current status of pest species. Given travel, importation, and climate change, new pest species can enter the environment, and old pest species can expand their range or increase population size at any given time. This can lead to increases in the use of pesticides already approved for a certain use, or the approval of previously-registered pesticides for new uses. A recent example is the brown marmorated stink bug, a native of Asia that was first detected in the US 10-15 years ago. Since its initial identification in Pennsylvania, the brown marmorated stink bug has expanded to 36 states and the District of Columbia as of February 2011. It is both a destructive pest to crops and a nuisance in commercial and residential areas. The effectiveness of currently registered pesticides is currently being tested to control its spread and damage.

National Land-Cover Dataset: EPA currently uses the National Land-Cover Dataset (NLCD), a product of the Multi-Resolution Land Characteristics Consortium comprised of several federal agencies, in its effects determinations for listed species. As described to the FWS, the NLCD is used to determine the geographic extent of land cover classes associated with pesticide use (e.g., geographic extent of landcover currently in agriculture). The NLCD has been updated irregularly, in 1992, 2001, and 2006. As the source of information for the geographical extent of crop data, FWS would like to institute a mechanism in which any update to this dataset would be checked for significant changes that would extend the area of possible effects (e.g., agriculture is occurring in new areas) and determine if these changes would result in effects to species that had not been previously considered as part of section 7 consultation. For land cover classes that do not change, reinitiation would not be needed. For land cover classes that change in either size or geographic extent from the dataset used in consultation, reinitiation may be necessary. EPA indicated that it was unable to revisit this part of the analysis until the next Registration Review cycle, effectively 15 years or more, due to resource constraints. The FWS believes that expansion of cropland may be putting species in harm due to unanticipated exposure to pesticides.

USDA Pesticide Use Datasets: The application of datasets maintained by USDA has been advocated for determining pesticide use scenarios that may be more realistic for assessing current and future effects to listed species. At present, maximum values with regard to application rates and frequency of use are used by EPA and the Services to produce an estimated environmental concentration. We have met several times with staff from USDA, who have spent considerable time examining their datasets for representative information to illustrate the type and extent of data available for analysis. These data were culled from pesticide use reporting in the state of California, one of the few states that requires this reporting from pesticide applicants and maintains such data. Information presented at these interagency meetings was similar to that presented to the panel at the November 3, 2012 public meeting. These data have shown that in

many cases, pesticides are not used at maximum label rates, and the amount and extent of use can vary by crop, location, and year. However, these data have also shown that pesticide use at the maximum labeled rate is not uncommon and cannot be wholly discounted. So far, we have not detected any geographic or temporal patterns from this data that would allow us to confidently limit the scope of our consultation, nor extrapolate to states where data collection did not occur. We look forward to continuing to examine whether data are or could become available that more precisely define the amount of pesticides applied.

When asked to use these data to comment on "typical" application practices, USDA cautioned that the tenets of integrated pest management encourage applicators not to think in terms of typical application schedules. Best practices involve the development of treatment plans that are specific to the crop, region, and weather, and vary based on biological monitoring and modeling of current pest threats. These factors can all result in variations in the timing or frequency of application, the application rate, and the selection of one or more pesticides (including tank mixes and products containing multiple active ingredients). USDA scientists indicated that predictions regarding these factors any more than two years in the future were unsupported by the data.

2. In the letter to Susan B. Hazen from the Services to EPA/OPP dated January 26, 2004, the Services stated that the approach used by EPA would produce reliable effects determinations. The committee understands that some aspects of the agreements reflected in this letter were invalidated by a federal court. Nonetheless, the committee would like to know if agreements noted in the letter would reduce conflicts between EPA and the Services, and how any shortcomings in the approaches noted in the letter are reflected in the charge to the committee.

We note EPA's consultation requests continue to cite the Overview document and Hazen letter as their basis for analysis. At the time of the Hazen letter, the Services had performed an analysis of a risk assessment process that had been described by EPA, but was conceptual in nature in that it had never been practically used to make an ESA-based effects determination. While the Services concurred at the time that the process described by EPA would reliably produce effects determinations that would appropriately identify actions that are not likely to adversely affect (NLAA) listed species, and would produce all information necessary to initiate formal consultation where appropriate, implementation of the process did not confirm this belief. The FWS review of two of EPA's first NLAA determinations found that the conclusions reached by EPA were not consistent with those of the FWS, and nonconcurrence letters were issued outlining the areas of disagreement with EPA's analysis (USFWS 2008; 2009a). The issues that we outline in these letters are amongst the same issues that were cited by the court and that are highlighted in the charge to the committee:

- Evaluation of data from the open literature
- Consideration of mixtures
- Consideration of inert ingredients
- Exposure modeling
- Sublethal effects
- Estimation of future use

Furthermore, in its review of 55 requests from EPA for initiation of formal consultation, the FWS found EPA's implementation of the process described in the Overview document produced no requests containing sufficient information to initiate consultation, contrary to its findings when assessing the conceptual process. A letter of insufficiency was issued by the FWS (2009b), requesting the following information:

- A complete list of all pesticide products;
- Information of formulations, recommended tank mixes, and any available toxicity data; and
- A characterization of a reasonable worst-case exposure scenario and range of exposures likely to occur to the various populations of the listed species or units of critical habitat, or portions thereof

In this letter, we also identified several areas agreed upon by the three agencies in a December 2007 meeting that required additional development of methodologies in order to fulfill EPA's section 7 requirements for pesticide registration activities. Specifically, we agreed to:

- modify existing modeling to ensure estimated environmental concentrations (EECs) represent worst-case scenario concentrations as a basis for making effects determinations;
- modify existing modeling to ensure EECs are adequately predictive in low-flow and off-channel habitats;
- develop methodology to account for future changes in use of pesticides (at least 15 years) in urban and residential settings;
- identify and develop exposure estimates required for an effects analysis for formal consultation;
- develop an approach for modeling EECs on a nationwide scale for Section 3 Registration Review;
- develop a methodology to adequately account for exposure to additional chemical ingredients in formulated products and environmental mixtures; and
- develop a methodology to incorporate information on sublethal effects in making Not Likely to Adversely Affect/Likely to Adversely Affect determination.

In addition to these issues outlined in our correspondence to EPA, the court also identified uncertainty regarding routes of exposure, LOCs, and surrogates as areas in need of clarification between the agencies. We agree with the court's findings that uncertainty remains regarding these issues and have posed them to this panel for review, and in fact, were amongst those topics previously identified in the Hazen letter as areas to work on jointly (i.e., the use of safety factors in better characterizing effects using surrogate species; testing of additional surrogate species; characterization of chronic effects; estimation of pesticide exposure for low-flow habitats such as ponds and vernal pools; pesticide exposure of wildlife through dermal and inhalation routes; and use of pesticide-specific data for the derivation of LOCs). The FWS believes that the Overview document can provide a foundation for future assessments and be modified to produce reliable effects determinations by EPA. However, based on our review of effects determinations produced by EPA, we believe the methods as described in the Hazen letter require further clarification and agreement between the agencies to meet the original intent. The issues that are the source of conflicts as described above were discussed in our interagency workgroup, at management levels, and now are substantially before the panel. It is the hope of the FWS that the

issues brought before the NRC panel will refine and improve upon the methodologies described in the Overview document and bring resolution to the differing interpretations by the agencies.

3. The committee's statement of task states that the two Services and EPA use "differing protocols pertaining to the type and character of scientific information that may be appropriate" as best available data. From your perspective, what is the most important difference between these protocols? Please illustrate this difference with an example.

We refer the committee to the section of our response for #1 regarding best available data.

4. Have there been new issues regarding the process to capture the best data as characterized in the 2004 Hazen Letter from FWS to EPA - page 13, 1st - 2nd paragraph?

Regarding species data, EPA presently contacts FWS field offices for species lists and range maps. Benchmark documents regarding species status and life history including Recovery Plans, Critical Habitat Designations, and Listing Packages are available on our ECOS website (<http://ecos.fws.gov/>). Since the Hazen letter, the FWS has increased the frequency of availability of its Five-Year Review documents, which summarize the most recent data available, and are also available online.

Regarding toxicological data, improvements have been made regarding transparency of the data EPA screens in preparation of their assessments. When delivering an effects determination to FWS, lists of all references screened for use in the assessment are provided, broken into the following categories:

- Studies that are acceptable for the ECOTOX database and acceptable by OPP for use in making an effects determination;
- Studies that are acceptable for ECOTOX but not acceptable by OPP; and
- Studies that are rejected by ECOTOX and OPP.

However, these lists can be quite extensive, especially for chemicals that have been registered for many years. Without adequate consensus on the use of literature in determining effects to species, a considerable burden is placed on the Service in reassessing the value of studies rejected for use by EPA. For example, in EPA's assessment of the risks of carbaryl to the Barton Springs salamander, the total list of references considered spanned 395 pages, citing 2116 individual references (USEPA 2007b). For atrazine, another long-registered pesticide, the list of references consisted of 309 pages (e.g., USEPA 2007a). Without prior agreement on which studies constitute the best available data, the Service must make a decision for each reference on the list as to whether it may contain relevant data, obtain those source documents, and determine whether the data contributes to the assessment of risk for listed species. Ultimately it is the role of the action agency (i.e., EPA) to use all relevant data in assessing risk to species. The transfer of burden to the Services is not only duplicative, but cannot be maintained under current statutory deadlines for the anticipated workload.

Similarly, when reviewing data from the open literature, EPA's Evaluation Guidelines for Ecological Toxicity Data in the Open Literature (May 9, 2011), risk assessors are to create a table of all endpoints derived from the open literature and identify studies that report more

sensitive or lower endpoints than the registrant-submitted guideline studies. As stated in a recent effects determination, in general, effects data in the open literature that are more conservative than the registrant-submitted data are considered" (USEPA 2011b). EPA selects the most sensitive endpoint for making the effects determination. This is adequate for a screening level determination that simply identifies if species face any potential risk. However, it falls short of describing the full range of responses an organism may experience at the EEC if other endpoints that falls within that range are not included. In order to determine if an action will jeopardize a listed species or adversely modify critical habitat, the Service requires a complete description of the manner in which the action may affect the listed species and their critical habitats, not solely the most sensitive effect that may occur. As above, the burden of reviewing these data and incorporating relevant endpoints into the effects analysis falls to the FWS

5. How are FIFRA required studies that are not published in the open literature regarded differently from other data from non-peer reviewed or unpublished sources? What constitutes "gray literature"?

FIFRA required studies that are not published in the open literature are evaluated by the Service in the same manner as all other potential sources of useful information. Evaluation is based on many of the same criteria that a peer reviewer for an open literature professional journal would use to evaluate a manuscript being submitted for publication. Such criteria include, but are not limited to examining the experimental design, the methods used for sampling and measuring data, the validity of controls and standards, the rigor of data QA/QC, applicability and general acceptance within relevant professional disciplines of quantitative analyses/interpretation of data, degree of internal and external replication, proper use of surrogates, degree of realism or transferability of study results to free-ranging organisms, and the overall logical soundness of reported conclusions relative to presented data and data analyses.

As per the Service's formal policy on information standards under the Endangered Species Act (FR, July 1, 1994 (Vol. 59), p. 34271; a copy of which can be found in the Services' joint Consultation Handbook at Appendix A, Item 3), "gray literature" is identified as "...status surveys, biological assessments, and other unpublished material... from State natural resource agencies and natural heritage programs, Tribal governments, other Federal agencies, consulting firms, contractors, and individuals associated with professional organizations and higher educational institutions." Examples of common forms of gray literature would include graduate student theses or dissertations, U.S. Geological Survey Open File Reports, U.S. Geological Survey Professional Papers, numerous different EPA Technical Report series and guidance documents, private sector reports from trade supported organizations such as the Water Environment Research Foundation (WERF) and Great Lakes Environmental Center (GLEC). The primary principle being that the Service does not pre-judge any potential source of information based on its "cover." All potential sources of information, whether it be published open literature or "gray literature," are evaluated solely on the rigor and soundness of their scientific content. Where a published open literature source is preceded by a thesis, dissertation, or other gray literature report, the Service's experience has often been that the dissertation or gray literature report is often more useful for section 7 consultation purposes because gray literature sources often have more expansive and detailed methods sections and often include extensive appendices of raw data that allow the Service to potentially use the data to address questions that are very relevant to section 7 consultation, but may not have been addressed in the published paper. Standardized peer review is a significant positive feature of published open

literature, but an accompanying negative feature from a section 7 perspective is the substantive space limitations of professional journals, such that in some regards published papers are almost extended abstracts and data summaries of the full length gray literature reports that often precede open literature publication.

No undue deference is afforded to the published open literature by the Service. As emphasized in the NRC/NAS "Reference Manual on Scientific Evidence" (National Academies Press, 2011: 48), one of the "Myths" about science is that... *"The institution of peer review assures that all published papers are sound and dependable."* While the "Fact" is that... *"Peer review generally will catch something that is completely out of step with majority thinking at the time, but it is practically useless for catching outright fraud, and it is not very good at dealing with truly novel ideas. Peer review mostly assures that all papers follow the current paradigm (see comments on Kuhn, above). It certainly does not ensure that the work has been fully vetted in terms of the data analysis and the proper application of research methods."* An excellent example of the fallibility of published open literature that is relevant to section 7 pesticide consultations is the notion that NOECs (no observed effect concentrations) bear any scientifically defensible relationship at all to safe concentrations of environmental contaminants. This notion has been commonly accepted in the published open literature and by EPA's pesticides programs for many years, but recently has been increasingly criticized as a *"...bankrupt statistical method in ecotoxicology..."* Even before recent publications by Landis and Chapman (2011a,b) and Fox (2011) presented such harsh professional judgments, the Service in biological opinions gave the NOEC concept the same "hard look" that we give all potentially relevant published and unpublished scientific information. Most recently, in the Service's January 15, 2010, draft biological opinion for EPA's Clean Water Act 304(a) criteria for cyanide we found that:

Decades ago Suter et al. (1987) reported that MATC's for fish fecundity, on average, corresponded to a 42% level of adverse effect (MATC = Maximum Acceptable Toxicant Concentration; a term for the geometric mean of the NOEC and LOEC from a given toxicity test and often assigned by EPA as the estimated "chronic value" from a test). Other response endpoints were found to correspond to average adverse effect levels of 12-35%. More recently, SETAC (Society for Environmental Toxicology and Chemistry) convened a panel of experts (Reiley et al. 2003) who concluded that *"...[toxicity] tests with high variability may result in an(sic) NOEC corresponding to a response greater than 40% different from the control."* Moore and Caux (1997) statistically examined nearly 200 toxicity data sets and found that most NOEC's (76.9%) exceeded a 10% adverse effect level and most LOEC's (62.4%) exceeded a 30% effect level. Various other researchers have noted a variety of adverse effect levels for NOEC's, such that Crane and Newman (2000) were led in summary to conclude that *"...[NOEC] effect levels from individual tests ranged from nearly 0% to nearly 100%."* For seven cyanide toxicity tests with sufficient data for comparison, Gensemer et al. (2007: Figure 3-7) found in all cases that the geometric mean of the NOEC and LOEC corresponded to an adverse effect level of $\geq 20\%$ (how much greater was not reported).

Because of the highly variable and often substantive levels of effect associated with NOEC's, LOEC's, MATC's, and with the "chronic values" based on them, and for numerous other reasons, a strong professional consensus recommendation to avoid using NOEC/LOEC-based estimates for regulatory thresholds (when possible) has been

expressed repeatedly. For example, there was an ISO (International Organization for Standardization) resolution (ISO TC147/SC5/WG10 Antalya 3) as well as an OECD (Organisation for Economic Co-operation and Development) workshop recommendation (OECD 1998) that the NOEC should be phased out from international standards (OECD 2006:14). Environment Canada (2005) notes, that there is a growing literature which points out many deficiencies of the NOEC approach (Suter et al. 1987, Miller et al. 1993, Pack 1993, Noppert et al. 1994, Chapman 1996, Chapman et al. 1996, Pack 1998, Suter 1996, Moore and Caux 1997, Bailer and Oris 1999, Andersen et al. 2000, Crane and Newman 2000, Crane and Godolphin 2000). Moving away from the NOEC/LOEC approach was also among the recommendations of the SETAC panel for improving the scientific basis of water-quality criteria (Reiley et al. 2003).

Subsequent to that hard look at a commonly accepted notion in the published open literature by the FWS even more forceful critiques have been published, most recently by Landis and Chapman (2011) calling for *"...regulatory agencies across the world to ban statistical hypothesis tests for the reporting of exposure-response from their guidance documents."* The Service suspects that the wider scientific community would predominantly agree with the Service's view that NOECs should not continue to be an EPA core basis for evaluating chronic risks posed to ESA-listed species by pesticides and we desire NRC advice on this issue.

In summary, the Service conducts a fully inclusive search for potentially relevant scientific information-- be it published or unpublished-- and subjects all categories of potential information, including FIFRA required studies, to take a "hard look." The FWS then makes decisions regarding incorporation of information into a biological opinion based solely on the scientific merit of the information based on best professional judgment. One of the key controls on this process is the requirement (FR, July 1, 1994 (Vol. 59), p. 34271; a copy of which can be found in the Services' joint Consultation Handbook at Appendix A, Item 3) that Service biologists fully document their evaluations of scientific information relied upon in a biological opinion and place any unpublished sources into the administrative record.

6. What is the Services' role at the problem formulation stage regarding data needs? Has Data-Call In (DCI) been used to fill critical data gaps on species- or habitat-specific data?

While FWS understands that EPA makes its registration review plan available on the federal register during the problem formulation stage, we are not specifically contacted by EPA for input when deciding on issues of data sufficiency for a pesticide undergoing registration review. As FWS understands the process, EPA compiles the registrant submitted studies and, if data gaps exist, makes a decision as to whether the registrant will be required to generate data to fill those gaps. EPA can choose to waive outstanding requirements if it is determined that studies exist in the open literature that would adequately assess risk to the endpoint identified in the data gap, or if the completion of these studies would otherwise contribute little or no value to the risk assessment.

While the FWS currently has no role at the problem formulation stage regarding data needs, we feel that this process could be improved if FWS and EPA collaborated on data needs for section 7 consultation as contemplated in the pesticide counterpart regulations (see 50 CFR 402.44). We base this belief on several examples of long-registered pesticides that underwent review through

EPA's reregistration or have been the recent subject of section 7 without key data requirements that the FWS believes are necessary to assess risk to listed species:

- Chlorophacinone, an anticoagulant rodenticide, was first registered in 1971. Birds may be exposed to chlorophacinone by direct consumption of bait, or via predation or scavenging of target species (e.g. mice, rats, prairie dogs, voles). In 2010, EPA initiated consultation on the effects of chlorophacinone used for black-tailed prairie control. Their analysis investigated potential effects to 8 listed avian species. At the time of this initiation and as the FWS currently completes the Biological Opinion, the data requirement for an avian reproduction study remains unfulfilled, 40 years after this pesticide's initial registration, limiting the ability to fully assess effects to avian species.
- Creosote, a wood preservative, has been constantly registered as a pesticide under FIFRA since 1948. Polycyclic aromatic hydrocarbons (PAHs), which can exert carcinogenic, teratogenic, and mutagenic effects both individually and in combination, comprise approximately 80% of the total make-up of creosote and account for its main toxicity. In 2004, FWS submitted a comment letter to EPA regarding its risk assessment of creosote, identifying 17 ecotoxicological data gaps that were cited in its risk assessment (USFWS 2004). Frequently asserting its inability to assess risk to wildlife, including fish and aquatic invertebrates which might be exposed to creosote via pilings, EPA nonetheless derived risk quotients with great uncertainty. Despite its potentially high toxicity, EPA made determination that creosote did not pose a risk to non-target plants and animals evaluated.
- Methyl parathion is an organophosphorus pesticide registered since the 1950's. In its 2004 comment letter, the FWS expressed concern about potential effects detailed by EPA for fish and wildlife in its Interim Reregistration Eligibility Decision. However, despite the known toxicity of this pesticide, chronic effects studies to fish could not be assessed due to a gap in the registrant-required data. This data gap was of particular concern to FWS as the NOEC derived for aquatic invertebrates was extremely low at 0.02 ppb.

7. How are incidence reports and investigative reports from other governmental entities (2004 Hazen Letter - page 11, 2nd bullet) taken into consideration in the effects determination?

Incident reporting can provide valuable information regarding exposure and effects of pesticides to nontarget species in the field. The FWS routinely reports incidents to EPA that have been handled either through our Law Enforcement or shared with our agency via other means. Analyses of carcasses collected from the field give us rare glimpses into the contaminant load carried by organisms and even when not diagnostically definitive, may provide information regarding exposure routes that are only considered hypothetically in a risk assessment. Incident reporting can also give us valuable information about pesticide misuse, an effect of the action that but for the pesticide registration would not occur. However, while we value incident reporting, we do not believe that an absence or low number of incidents is indicative of an absence of effects to wildlife. To assume that the absence of effects implies that no effects exist makes the error of the null fallacy, which mistakenly gives a null finding equal weight to a positive finding (Hamilton and Lemly 1999). A null finding – in this case the absence of carcasses – provides evidence neither for nor against effects to wildlife. However, incident reporting can be a useful mechanism by which to draw attention to the unintended consequences

of pesticide use, distinguish the magnitude of the problem as compared to other pesticides, and elucidate the probable exposure routes causing the effect.

Any incidents reported are likely to represent only a fraction of the actual mortality for any given pesticide (Vyas 1999). In order to document a pesticide-related mortality, a carcass must be observed, reported, collected, and chemically analyzed while still relatively fresh. Carcass-detection studies have found that even when searches are performed on known carcasses, a significant percentage will never be found due to scavenging, location in remote, inaccessible areas, or size or coloration that renders the carcass inconspicuous (Vyas 1999). Some pesticides exhibit delayed toxicity, which can temporally or geographically distance the carcass from the application area, further masking a connection to the pesticide exposure (Colvin et al. 1988). In addition, exposure to pesticides may result in sub-lethal effects that occur at concentrations below a diagnostic threshold for lethality, masking their role in mortality incidents where acute mortality from is not the proximal cause of death but may have contributed to other causes such as trauma or disease (Stone et al. 1999).

While detecting carcasses in the field is rare, regularly detecting effects other than mortality that can be successfully tied to pesticide use is nearly impossible. As newer chemistries are developed for pesticides, effects to nontarget species have gravitated from overt effects such as mortality or eggshell thinning, to sublethal effects such as endocrine disruption, behavioral modifications, and immunosuppression. These effects may manifest to be equally as harmful to species, but without the benefit of a "smoking gun" such as a carcass or cracked eggshell, detecting these effects in the wild requires controlled monitoring beyond which we have the capability to carry out. In addition, due to the multiple pollutant stressors occurring in almost any habitat of a listed species, teasing out these effects and attributing them to one or more stressors causes considerable challenge. Because of this difficulty in detecting both carcasses and other adverse effects in the field, it is critical that we recognize the potential for adverse effects of any nature upfront, consider the potential consequences to species, and properly mitigate to relieve these effects. The history of FIFRA implementation has shown that once a pesticide is registered, the burden of proof shifts to proving the existence of adverse effects in the wild, which as discussed, is a high bar to surmount.

8. In your experience, have new data crucial to refining the effects determination become available after the draft environmental risk assessment is released?

Data are constantly being generated from researchers at universities, government agencies or private institutions that address effects of pesticides upon fish and wildlife. Because these data generally addresses endpoints, species, or exposure scenarios that expand upon the requirements for pesticide registration, they must be considered for information this is novel or otherwise important to the risk assessment. The FWS typically does not review the draft risk assessment, rather gets a final effects determination from EPA for the initiation of consultation. However, we can identify examples of seminal data that have become available either during EPA's preparation of its effects determination or after its submission to FWS that would significantly impact the risk assessment.

- In EPA's effects determinations for atrazine, chronic effects to fish were analyzed using a NOEC concentration of 65 ug/L, based upon reduced growth to brook trout (USEPA 2006;

2007c; 2007d; 2009a). In 2010, USGS scientists published their findings of reproductive effects of atrazine to rainbow trout at 0.05 ug/L (Tillitt et al. 2010). This value is 130 times lower than the NOEC value used by EPA in its assessments and below both monitored environmental concentrations and EECs calculated in all of the above referenced effects determinations. Though not published until 2010, data describing these effects were first presented at the Society of Environmental Toxicology and Chemistry meeting in 2006 (Papoulias et al. 2006a; Papoulias et al. 2006b), and an early draft of the manuscript was provided to EPA (D. Tillitt, USGS, personal communication). This study has not yet been used to assess effects to listed species.

- In EPA's 2010 effects determination for the registration of Rozol prairie dog bait, birds were assessed for their potential effect from exposure to the inandione rodenticide chlorophacinone. As no toxicity data for raptors were available, risk was assessed using LD50 from bobwhite quail. In 2010 and 2011, studies were published indicating that the acute toxicity of American kestrels (*Falco sparverius*) to diphacinone, a closely related inandione rodenticide, was over 20 times more sensitive than northern bobwhite and over 30 times more sensitive than mallards (*Anas platyrhynchos*), the two test species required by the EPA for pesticide registration (Rattner et al. 2010a and 2011b). Given the similarity of the pesticides and the potential for much greater risk to listed raptors than anticipated, FWS considered this data in developing its Biological Opinion and encourages EPA to integrate this information into future assessment.

9. The Services and EPA have used differing approaches on how to characterize indirect, sublethal, and cumulative effects. From your perspective, what is the most important difference between these approaches with respect to each (or all) of these effects? Please illustrate with examples.

We refer the committee to our response for sublethal, indirect, and cumulative effects under Question #1.

10. If your agency uses population models to evaluate potential impacts of pesticides on threatened and endangered species, do these models incorporate (i) density dependence, (ii) spatial structure, (iii) temporal variability in model parameters, or (iv) uncertainty (i.e., measurement error) in estimated values of model parameters? If so, please provide an example of how each of these factors have been incorporated into a model, and how the relevant parameters were estimated.

The FWS has not yet completed a pesticide biological opinion on an ESA-listed species for which sufficient data were available to consider utilizing population models. This "data-poor" circumstance is the typical state of knowledge for the vast majority of ESA-listed species for which the FWS has section 7 responsibilities. Our species are typically non-commercial species that have been subject to limited demographic and life history population studies, if any at all. We expect that formal population models will only very rarely be a tool that can be utilized to inform our pesticide biological opinions. At such time as the FWS has the luxury of utilizing population models any NRC advice/guidance on this topic will be fully implemented to the extent that it can reasonably be accomplished. The FWS will also closely monitor and incorporate best scientific practices and lessons learned as illustrated by the use of population

models applied in precedent setting section 7 consultations for data-rich commercially important species such as salmonids.

11. If, after an initial evaluation, it is determined that potential jeopardy exists, what approaches can be used to make site-specific evaluations? In this context, site-specific means evaluating the effect of a pesticide only within the range and the specific habitat of the threatened or endangered species that might be impacted by the specific action.

The utility of site-specific evaluations to avoid jeopardy or adverse modification would depend greatly on the circumstances leading to that determination. In the case of species with a relatively narrow distribution, imposing a site-specific limitation on use of the product (e.g., lower rate, buffer area, fewer applications) could serve to avoid jeopardy for the species in question without unduly limiting the use of the product elsewhere. For more wide-ranging species and for products that may affect hundreds of species such site-specific approaches may be too challenging. Greater utilization of "County Bulletins" may enable EPA to be more geographically precise in implementing controls on pesticide usage.

12. What is the current progress in collectively developing methods to increase the confidence of using surrogate species data (see 2004 Hazen Letter from FWS to EPA – page 14-15)?

There has been no progress towards collectively developing methods to increase the confidence of surrogate species data. The Workgroup did not progress to the point of addressing this topic. However, we address the subject of surrogate species and related uncertainties in our response to questions 21.

To increase confidence in using surrogate data, the FWS has long advocated for the inclusion of additional test species to better represent taxa of listed species. Specifically, we find the most tenuous use of data to be extrapolation of birds and fish to amphibians, daphnia to mussels, birds to reptiles, and the mallard or quail to raptors. Absent registrant-submitted data from species within these taxa, we advocate use of data from the open literature, the use of safety factors to address the uncertainty in extrapolating the effects of pesticides across taxa, and the use of data from closely related chemicals where meaningful extrapolations can be made to under-represented species.

13. How do you define the baseline condition when considering re-registration of a pesticide, given that the article in question has been used in the environment for 10+ years and is not a new stressor?

In this context the "baseline condition" is the "Status of the Species" as it exists at the time of the re-registration, which includes the past use of the registered pesticide plus all other factors that have impinged on the species up to that point. We then characterize the "Effects of the Action" by estimating what we think the status will be in the future without continued use of the pesticide versus with use of the pesticide.

A section 7 analysis considers the future effects of an action on the status of the species and its critical habitat. The "effects of the action" are, in part, defined by the scope of an agency's

action and their discretion. Although a pesticide may have been in use for 10+ years, continued use of the pesticide is not the proper basis for comparing the effects of the action.

14. How do you integrate life history information of the species (in particular, the amount of time, the time of the year, and the life stage that is spent in locations where pesticide exposure may occur) with estimates of residue concentrations in environmental or biotic media over space and time?

The FWS's "Advanced Interagency Consultation" course materials provide a study guide for completing exposure analyses (see attached). In short, the FWS would identify the timing, location, frequency, duration, and intensity of the stressors associated with the action; then characterize the physical and biotic features that may be exposed, the life stages or forms of the listed species that may be exposed, the number of individuals that may be exposed, and the populations that may be exposed. A similar analysis is completed for the physical and biological features of critical habitat that may be exposed.

QUESTIONS FOR FISH AND WILDLIFE SERVICE

General Questions

20. Considering the date of the interagency "Consultation Handbook" (March 1998) what additional current guidance, if any, does your agency provide, in practice, for the consultation process?

The Consultation Handbook is the guiding document for the Services. It provides internal guidance and establishes national policy for conducting consultation and conferences pursuant to section 7 of the Endangered Species Act (ESA) of 1973, as amended. The purpose of the handbook is to provide information and guidance on the various consultation processes outlined in the Act (section 7) which are further developed in regulations (50 CFR §402) and to promote efficiency and nationwide consistency within and between the Services. Although primarily targeted toward employees of the Services, the Consultation Handbook can be used as a reference guide to other groups participating in the consultation process by providing an explanation of the section 7 processes and providing examples of various types of consultations. It is recognized in the handbook that periodic updates will occur if the Act is amended, as new regulations and policies are developed affecting implementation of the section 7 regulations or as new consultation or assessment techniques evolve.

When hiring new employees for the purpose of conducting section 7 consultations, the FWS requires those employees to take formal training entitled "Interagency Consultation for Endangered Species" provided through the FWS National Conservation Training Center (NCTC). This weeklong course was developed by the FWS, but is often attended by NMFS employees and employees of other agencies who have an interest in learning more about the consultation process. On a periodic basis, an advanced course in interagency consultation is offered through NCTC.

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The FWS developed a course, "Developing a Biological Assessment," targeted specifically at action agencies in an effort to improve the quality of analysis submitted for consultation. The course guides the action agencies on how to write an adequate biological assessment or biological evaluation that fulfills the requirements of section 7 of the ESA.

The FWS also has a process of sharing information, guidance, or policy on consultation issues among the national, regional and field offices through regular communications among a team of national and regional section 7 coordinators. Monthly coordination calls are conducted between the national and regional coordinators and between the regional coordinators and field staff. Consultation teams at the field and regional levels may be used to provide consistency across offices for particular listed species of interest. For instance, the FWS has approximately 10 field offices that conduct northern spotted owl consultations. In an effort to improve consistency across offices, the FWS has a northern spotted owl consultation coordination team that meets quarterly to discuss current issues and develop products (e.g., status of the species) that are used across offices in biological opinions.

Since the inception of the Consultation Handbook, new directives and regulations have been issued by the Service regarding consultation procedures. On August 6, 2004 the Ninth Circuit Court of Appeals rendered a decision in *Gifford Pinchot Task Force v. U.S. Fish and Wildlife Service*, No. 03-35279, finding that the FWS regulatory definition of "destruction or adverse modification" of critical habitat, at 50 CFR §402.02, is contrary to law. Previous Federal court rulings had reached similar conclusions. In light of these rulings, the FWS issued a Director's Memo, "Application of the 'Destruction or Adverse Modification' Standard under Section 7(a)(2) of the ESA" (FWS 2004) to provide guidance on an analytic framework to make "destruction or adverse modification" findings in biological opinions. In essence, biological opinions issued after December 9, 2004 no longer rely on the regulatory definition of "destruction or adverse modification" of critical habitat at 50 CFR §402.02, but instead rely on the statutory provisions of the ESA to complete the "destruction or adverse modification" of critical habitat analysis.

Additionally, the FWS, NMFS and EPA promulgated Joint Counterpart ESA Section 7 Regulations (Counterpart Regulations) (50 CFR §402, Subpart D) and signed an Alternative Consultation Agreement for Implementation of Optional Alternative Consultation Procedures (ACA) (EPA et al. 2004).

In August 5, 2004, Counterpart Regulations (50 CFR §402, Subpart D) were finalized for regulatory actions under FIFRA. These Counterpart Regulations were intended to enhance the efficiency and effectiveness of the section 7 consultation process by increasing interagency cooperation and providing two optional alternatives for completing section 7 consultation for FIFRA regulatory actions. Generally, the Counterpart Regulations outlined procedures for interagency exchanges of information, advance coordination for FIFRA actions (i.e., the EPA could request a FWS representative to work with EPA in developing effects determinations), alternative consultation on FIFRA actions that are not likely to adversely affect listed species or critical habitat (i.e., allows the EPA to make NLAA determinations without informal consultation or written concurrence from the FWS), optional formal consultation procedures for FIFRA actions (i.e., this allows EPA to use a FWS representative during the development of an

effects determination, thus foregoing the ability of the FWS to request additional information on a proposed action once a formal request for consultation has been received from the EPA), special consultation procedures for complex FIFRA actions (i.e., allows EPA to address the effects of an action through successive effects determinations; the FWS provides partial opinions), and conference on proposed species or proposed critical habitat. Additionally, the Counterpart Regulations allow EPA to conduct emergency consultations on actions involving emergency exemptions under section 18 of FIFRA.

On August 24, 2006, a District Court ruled in *Washington Toxics Coalition vs. U.S. Department of the Interior, U.S. Fish and Wildlife Service, U.S. Department of Commerce and National Marine Fisheries Service*, that the NLAA (50 CFR §402.45) and emergency consultation provisions [50 CFR §402.42(a)(6)] issued by the Federal Defendants in Counterpart Regulations (50 CFR §402, Subpart D) (August 5, 2004) were arbitrary and capricious, and contrary to law and set aside these provisions. In making its ruling, the Court conducted a lengthy review of EPA's Overview Document and our collective administrative record and highlighted the many differences between EPA's risk assessment process and the process that the Services use to make effects analysis and determinations in their biological opinions. The Court stated "EPA's risk assessment process is not only less protective than Service determinations, there is overwhelming evidence on the record that without a Service check, EPA risk assessments (leading to pesticide registrations) would actually result in harm to listed species."

21. What is your definition of a surrogate species? Has the definition of surrogate species changed in response to literature on how well (or how poorly) surrogate species represent other taxa?

We consider surrogate species as species whose responses to toxicants are likely to be most similar to that of the listed species and for which toxicity data are available. We assume that species that are taxonomically related to the listed species will have similar physiologies and thus be better suited for estimating toxic responses. We also consider species which share similar life history characteristics with the listed species as preferred surrogates for estimating population-level effects. We assume that population-level responses to toxic effects on individuals would be most similar for species which share life history characteristics (e.g. reproductive strategies: r- and K-selected species).

We have learned from the literature, including technical documents, that there can be a high degree of interspecies variability in responses to toxic chemicals and that, among chemicals, no single species is always the most or least sensitive (Meyer and Ellersink 1986). As a result, it is difficult to have confidence that the response of an individual surrogate species adequately represents the sensitivity of the many untested listed species. Dwyer et al. (2005) investigated this experimentally by comparing the responses of listed fish species with common fish surrogates. They conducted acute toxicity tests with 5 chemicals and 19 fish species, including 16 listed or closely related species and 3 commonly tested fish species (i.e. rainbow trout, fathead minnow, and sheepshead minnow). Toxicity values (LC50) varied among species, from 5X to 22X depending on the chemical. Rainbow trout, often considered to be a "sensitive species", ranked 6th overall (range 5th to 11th) in sensitivity. Fish from 3 of the 7 families tested tended to be more sensitive than rainbow trout, illustrating that even "sensitive surrogates" may underestimate the responses of some listed species. Similar concerns have been raised regarding the use of surrogate species for extrapolating from individual to population-level effects (Stark et

al. 2004, Banks et al. 2010). These examples from the literature indicate that we must not only be cautious in selecting surrogate species but also in how we use them for estimating effects to listed species. It may be necessary to extrapolate beyond the available data, using species sensitivity distributions or uncertainty factors for example, to arrive at estimates that minimize the likelihood of Type II error.

22. Please illustrate the process by which surrogates are selected and validated. Please present your transparent, repeatable method for identifying and validating surrogates, if applicable, and illustrate how the method was applied to two species with different life histories or habitat requirements.

As stated in response to question 21, we select surrogate species whose responses to toxicants are likely to be most similar to that of the listed species. We assume that species that are taxonomically related to the listed species will have similar physiologies and thus be better suited for estimating toxic responses. For example, the order of preference for selecting among available data would be species within the same genus, followed by family then order. Because we lack toxicity data for most listed species under our jurisdiction, it would be difficult to validate the accuracy of all surrogate-based estimates. The limited data we do have for listed fish has shown that some species are more sensitive to certain pollutants than commonly tested surrogates, including those often considered to be "sensitive", i.e. rainbow trout (Dwyer et al. 2005). Alternatively, we can take into account uncertainties associated with such estimates to reduce the likelihood of Type II error, that is, falsely concluding that a listed species will not be affected when in fact it will be. We believe that the greater the taxonomic distance between a listed species and their surrogates the more difficult it is to prevent such error (e.g. using fish and birds as surrogates for amphibians). In such cases there may be too much uncertainty to reasonably estimate effects and it may be necessary to collect new data on more representative species/taxa. A similar situation with freshwater mussels and the ammonia illustrates this point. Recent studies have revealed that young mussels are highly sensitive to the common water pollutant ammonia (Augsburger et al. 2003, Wang et al. 2007), more sensitive in fact than the species used to derive the national CWA 304(a) water quality criteria for ammonia (USEPA 1999). Prior to the new mussel toxicity data, mussels were not represented in the ammonia criteria data set and the most sensitive species belonged to several genera of fishes. The criteria derived using those sensitive fish genera were intended to be protective of freshwater aquatic life including taxonomically distant mussels. However, the 1999 ammonia criteria values are substantially higher than what is currently believed to be protective for mussels and EPA is in the process of revising the ammonia criteria to include mussel toxicity data (USEPA 2009b). In retrospect the 1999 ammonia criteria is an example of Type II error with respect to protection of freshwater mussels and the error would have gone undetected but for the willingness to test yet untested species and lifestages.

Questions for National Coordinator for Interagency Consultation at FWS

23. What type of guidance or training materials are provided to FWS personnel for how to deal with uncertainty when conducting Section 7 consultations?

Guidance to the FWS on uncertainty is provided through the consultation handbook. The consultation handbook is a compilation of information derived from the ESA, the implementing regulations, Congress reports, and court rulings.

The FWS currently relies on the best available scientific and commercial data available for determining potential effects of a proposed action that may lead to a determination of jeopardy for a listed species or adverse modification for critical habitat. When there is uncertainty in existing data or uncertainty due to significant data gaps, the FWS gives the benefit of the doubt to the species [H.R. Conference Report No. 697, 96th Congress, 2nd Session 12 (1979)]. During the formal consultation process, if the FWS determines that there are significant data gaps, it may ask the action agency to conduct additional studies. If the action agency declines to do so, the FWS will develop the biological opinion with the available information giving the benefit of the doubt to the species (see Handbook, pg 1-7).

When the U.S. Congress amended the ESA in 1979, both the House and the Senate debated the proper course of action the Services should take when writing biological opinions in the face of uncertainty; that is, when action agencies "cannot guarantee with certainty that the agency action will not jeopardize the continued existence of the listed species or adversely modify its critical habitat: [H.R. Conference Report No. 697, 96th Congress, 2nd Session 12 (1979)]. The Congress amended the ESA to allow the Services to frame our biological opinions on the best evidence that is available or can be developed during the consultation process and concluded that the language "continues to give the benefit of the doubt to the species, and it would continue to place the burden on the action agency to demonstrate to the consulting agency that its action will not violate Section 7(a)(2)" [H.R. Conference Report No. 697, 96th Congress, 2nd Session 12 (1979)].

The 1979 Conference Report also states that, when the information available does not allow the Services "to guarantee with certainty that the agency action will not jeopardize the continued existence of listed species," the U.S. Congress expected the Federal agency to have "a continuing obligation to make a reasonable effort to develop that information" [H.R. Conference Report No. 697, 96th Congress, 2nd Session 12 (1979)].

Congress' intent to provide the benefit of the doubt to the species has been referenced in the legislative history by incorporation into the preamble of the implementing regulations and by reference to the subject matter in numerous court rulings.

24. Is there an expectation of a standard approach across the Service for dealing with uncertainty when conducting endangered species assessments?

The expectation of FWS employees is to follow the guidance in the consultation handbook. Congress' intent to give the benefit of the doubt to the species in the face of uncertainty is reflected in the following statement: situations with high uncertainty, we often rely on adaptive management approaches. A key missing element in the pesticide regulation process is feedback from monitoring information that would serve to inform such adaptive management approaches. Without such feedback it is hard to evaluate the validity of assumptions and whether the process is achieving its intended goals (i.e., no adverse effect on the environment) and to make needed adjustments to improve the efficacy of the process.

25. *Do you commonly distinguish between natural biological variability, stochasticity in environmental metrics (such as climate), and lack of knowledge about a species when assessing the likelihood of extinction under different impact scenarios during Section 7 consultations?*

In biological opinions (opinions), the FWS is assessing whether the proposed action will reduce appreciably the likelihood of survival and recovery, not whether the proposed action would result in extinction. The FWS regards the section 7 consultation process as a "risk assessment" where we first ask whether the proposed federal action will have any effects to any individuals of listed species (or any aspects of their critical habitat), then whether those effects are adverse, and then finally whether those effects are so adverse as to be inconsistent with the conservation needs of the species. The regulations (50 CFR §402) define "jeopardize the continued existence of" as to "engage in an action that reasonably would be expected, directly or indirectly, to reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of that species." Actions that result in jeopardy to a species will generally increase the likelihood of extinction and as a species moves closer to extinction, the species can tolerate less risk. If the FWS reaches a jeopardy conclusion, the next step is to work with the agency proposing the action and to determine a different Reasonable and Prudent Alternative (RPA) that can be implemented to avoid jeopardy.

We often incorporate listing packages or recovery plans (by reference) into opinions where we commonly do an analysis of biological variability and stochasticity under the FWS 5-factor analysis. This information is typically found in the status of the species; a characterization of the rangewide status. In our characterization of a species' status, we would typically describe what we know of natural biological variability, stochasticity, vulnerability to stochastic events and our current lack of knowledge of a species; these are relevant considerations that establish the species' status (i.e., its current likelihood of extinction). Information within the status of the species section of an opinion would typically be narrowed down to focus on the species' life history traits and survival and recovery needs that would be potentially affected by the proposed action. These would be discussed in length for the particular consultation. For projects of short duration and local extent, concerns about stochasticity and lack of knowledge tend to be of limited concern but these factors become much more significant for consultations with broad geographic scope and long duration?.

With the evaluation of the status of the species the FWS is able to determine the species' current risk of extinction on a continuum between extinction and recovery. As we analyze various impact scenarios (e.g., different levels of pesticide exposure) in our effects analysis, we are trying to determine to what degree those scenarios will influence the extinction risk. The FWS consequently, needs to determine what level of risk is acceptable. When uncertainties exist, the FWS relies on the guidance to provide the benefit of the doubt to the species and in these cases we are less likely to accept risk. For example, the black-footed ferret is critically endangered. In the current consultation for registration of Rozol Prairie Dog Bait (chlorophacinone; an anti-coagulant) the FWS is willing to accept very little risk to the species and therefore worked with EPA and the registrant to place restrictions on the use of Rozol within its range.

To determine if the proposed action is likely to jeopardize the continued existence of a listed species, the FWS reviews the current status of the species (i.e., the likelihood of extinction), which evaluates the species' range-wide condition, the factors responsible for that condition, and its survival and recovery needs; the environmental baseline for the action area, which evaluates the condition of the species in the action area, the factors responsible for that condition, and the role of the action area in the species' survival and recovery; the effects of the proposed action and any cumulative effects. If the proposed action is determined to appreciably reduce the survival and recovery of the species and therefore increase the likelihood of extinction, then a jeopardy decision is warranted.

26. Please describe the formal or informal internal QA/QC and the external peer review processes for all critical assessments and determinations. Specifically, what type of internal QA/QC review is required for BiOps prepared under Section 7 consultations?

Internal Review

Internal review of biological opinions (opinions) within process, whether at the field, regional, or national level. the scope, complexity and degree of controversy of the p

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Each office within the FWS will have a standard procedure for review and signature of opinions. Jeopardy or adverse modification opinions will have a higher level of review than non-jeopardy and non-adverse modification opinions. Staff level biologists typically write opinions. They are educated in the biological sciences, often have advanced degrees, and have had formal training in section 7 consultation through the FWS National Conservation Training Center. Generally, at the field level, a staff biologist writes the opinion; the opinion is reviewed by the staff's immediate supervisor or Program Manager and then reviewed and signed by the Project Leader or Field Supervisor for non-jeopardy and non-adverse modification opinions. Jeopardy and adverse modification opinions are signed at the regional level and require an early alert (discussed below). At the regional level, a staff biologist writes the opinion, their immediate supervisor or Program Manager reviews the opinion, the Assistant Regional Director reviews the opinion, and finally the Regional Director reviews and signs the opinion. At the Washington Office, a staff biologist writes the opinion. The opinion is reviewed by the Branch Chief, Division Chief, and Deputy Assistant Director, then reviewed and signed by the Assistant Director for Endangered Species. Highly controversial opinions may be reviewed and signed by the Director. Early alerts are required for jeopardy and adverse modification opinions.

Jeopardy and adverse modification opinions require an early alert to the Director. The consultation handbook provides specific guidance as to handle these early alerts. The FWS Regional Directors provide the Washington Office with an early alert to inform the Director of both draft and final biological opinions, preliminary biological opinions (early consultation), and conference opinions of regional or national significance likely to result in findings of jeopardy or adverse modification. The Region submits such alerts as soon as biologists have completed the necessary analysis to determine if a jeopardy biological opinion or conference opinion is warranted and consultation with the federal agency/applicant has been unsuccessful in avoiding the jeopardy determination. Additionally, Regional Directors are encouraged to advise the Director of potentially controversial consultations before an early alert is required.

The early alert is submitted to the Chief, Division of Endangered Species. The Division of Endangered Species prepares a cover memo and forwards the early alert to the Assistant Director for Endangered Species, who forwards it to the Director. Regional Directors must first send in an early alert to the Washington Office and obtain approval from the Director before signing any draft and final biological opinions, preliminary biological opinions (early consultation), and conference opinions of regional or national significance likely to result in findings of jeopardy or adverse modification.

Peer Review

Peer review is not required under section 7(a)(2) of the ESA. Formal consultations have a statutory timeframe of 135 days for completion. This timeframe does not allow the opportunity for a formal peer review process initiated by the FWS. However, a consultation extension can be granted by the action agency if peer review is desired on a draft opinion. On rare occasions, external peer review has been requested by the FWS on highly complex or controversial projects and occasionally the FWS will seek legal review from our Solicitors Office.

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Preface

Under the US Endangered Species Act (ESA), the Fish and Wildlife Service (FWS) and the National Marine Fisheries Service (NMFS) are responsible for designating species as endangered or threatened (that is, listing species) and determining whether federal actions might jeopardize the continued existence of a listed species or adversely affect its critical habitat. Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the US Environmental Protection Agency (EPA) is responsible for registering pesticides and ensuring that pesticides do not cause unreasonable adverse effects on the environment, which includes listed species and their critical habitats. Over the years, EPA, FWS, and NMFS have struggled unsuccessfully to reach a consensus on approaches to assessing the risks to listed species. Consequently, EPA, FWS, NMFS, and the US Department of Agriculture (USDA) asked the National Research Council to examine scientific and technical issues related to determining risks to species that are listed under the ESA posed by pesticides that are registered under FIFRA.

In this report, the Committee on Ecological Risk Assessment under FIFRA and ESA first provides a common approach that EPA, FWS, and NMFS could use to conduct assessments. It then discusses models, data, and uncertainties associated with exposure analysis and addresses various issues associated with assessing the effects of pesticides on listed species, including evaluating sublethal, indirect, and cumulative effects; modeling population-level effects; considering the effects of chemical mixtures; and incorporating uncertainties into the effects analysis. The committee closes by discussing the risk-characterization process and the need to propagate uncertainty through all components of the assessment so that decision-makers are well informed regarding the risk estimates produced.

The present report has been reviewed in draft form by persons chosen for their diverse perspectives and technical expertise in accordance with procedures approved by the National Research Council Report Review Committee. The purpose of the independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards of objectivity, evidence, and responsiveness to the study charge. The review comments and draft

manuscript remain confidential to protect the integrity of the deliberative process. We thank the following for their review of this report: Steven Bartell, Cardno ENTRIX; May Berenbaum, University of Illinois; Nancy Bryson, Holland & Hart, LLP; Francesca Dominici, Harvard School of Public Health; Scott Ferson, Applied Biomathematics; Robert Gilliom, National Water Quality Assessment Program, USGS; Tilghman Hall, Bayer CropScience; Jeffrey Jenkins, Oregon State University; Andreas Kortenkamp, Brunel University; Bernalyn McGaughey, Compliance Services International; Anke Mueller-Solger, California Delta Stewardship Council; Terrance Quinn, University of Alaska Fairbanks; Joseph Rodricks, ENVIRON; Kenneth Rose, Louisiana State University; and Janet Silbernagel, University of Wisconsin, Madison.

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of the report was overseen by the review coordinator, Danny Reible, The University of Texas at Austin, and the review monitor, Michael Ladisch, Purdue University. Appointed by the National Research Council, they were responsible for making certain that an independent examination of the report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of the report rests entirely with the committee and the institution.

One committee member, Daniel Goodman, disagreed with the committee on several points and prepared a dissenting statement that was included as an appendix in the draft report that was submitted to peer reviewers. The report has been substantially revised in response to reviewer comments, and many issues raised by Dr. Goodman have been addressed with changes to the report. However, Dr. Goodman passed away while the report was in review, so determining how he would have judged the revised report is not possible. Accordingly, his dissenting statement has not been included in this final report; however, it is available in the public access file.

The committee gratefully acknowledges the following for their presentations to the committee during open sessions: Ann Bartuska, David Epstein, and Harold Thistle, USDA; Steven Bradbury and Edward Odenkirchen, EPA; Aimee Code, Northwest Center for Alternatives to Pesticides; Nancy Golden, FWS; Christian Grue, University of Washington; Barbara Harper, Confederated Tribes of the Umatilla Indian Reservation; Scott Hecht and Nathaniel Scholz, National Oceanic and Atmospheric Administration; Jeffrey Jenkins, Oregon State University; Steve Mashuda, Earthjustice; Bernalyn McGaughey, Compliance Services International; John Stark, Washington State University; and Mike Willett, Northwest Horticultural Council. The committee members also thank the staff of EPA, FWS, and NMFS for being so helpful in answering their numerous questions throughout the study process. It especially thanks Jim Cowles, formerly of the Washington State Department of Agriculture, and Scott McMurry, Oklahoma State University, for their useful input in the early deliberations of this study.

Preface

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The committee is grateful for the assistance of the National Research Council staff in preparing this report. Staff members who contributed to the effort are Ellen Mantus and David Policansky, project codirectors; Keri Stoever, research associate; James Reisa, director of the Board on Environmental Studies and Toxicology; Norman Grossblatt, senior editor; Mirsada Karalic-Loncarevic, manager of the Technical Information Center; Radiah Rose, manager of editorial projects; and Craig Philip, senior program assistant.

I especially thank the members of the committee for their efforts throughout the development of this report.

Judith E. McDowell, *Chair*
Committee on Ecological Risk
Assessment Under FIFRA and ESA

Dedication

This report is dedicated to Dr. Daniel Goodman (1945-2012), who served on the committee that authored this report until November 14, 2012, when he passed away unexpectedly. Dr. Goodman was professor and director of the Environmental Statistics Group in the Department of Ecology at Montana State University in Bozeman, where he had been on the faculty since 1980. Dr. Goodman provided advice to several federal agencies, including NOAA and EPA, and had served as a report reviewer for the NRC before becoming a member of this committee. The committee and the NRC are grateful for his service and his contributions.

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ASSESSING RISKS TO
Endangered and
Threatened Species
FROM
PESTICIDES

Summary

Under the Endangered Species Act (ESA), the US Fish and Wildlife Service (FWS) and the National Marine Fisheries Service (NMFS)—herein called the Services—are responsible for listing species as endangered or threatened and for designating critical habitats that are essential for their conservation. Furthermore, in consultation with the Services, federal agencies must ensure that their actions are not likely to jeopardize listed species or adversely affect critical habitats. Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), the US Environmental Protection Agency (EPA) is responsible for registering or reregistering pesticides and must ensure that pesticide use does not cause any unreasonable adverse effects on the environment, which is interpreted to include listed species and their critical habitats. The agencies have developed their own approaches to evaluating environmental risk, and their approaches differ because their responsibilities, institutional cultures, and expertise differ. Over the years, the agencies have tried to resolve their differences but have been unsuccessful in reaching a consensus regarding their assessment approaches. As a result, FWS, NMFS, EPA, and the US Department of Agriculture asked the National Research Council (NRC) to examine scientific and technical issues related to determining risks posed to listed species by pesticides. Specifically, the NRC was asked to evaluate methods for identifying the best scientific data available; to evaluate approaches for developing modeling assumptions; to identify authoritative geospatial information that might be used in risk assessments; to review approaches for characterizing sublethal, indirect, and cumulative effects; to assess the scientific information available for estimating effects of mixtures and inert ingredients; and to consider the use of uncertainty factors to account for gaps in data. The present report, which was prepared by the NRC Committee on Ecological Risk Assessment under FIFRA and ESA, is the response to that request.

THE FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT AND THE ENDANGERED SPECIES ACT

FIFRA is the federal statute that governs the sale, distribution, and use of pesticides in the United States; it assigns EPA the authority to issue pesticide registrations or reregistrations, which are required for use of the pesticides. To obtain a registration, an applicant must demonstrate that a pesticide will perform

its intended function and will not cause unreasonable adverse environmental effects. Once granted, the registration requires that the pesticide be labeled with specific product information, directions for use, and hazard information; the label specifies legal use of the pesticide.

The ESA is the federal statute that assigns FWS and NMFS the authority to designate species as threatened or endangered—that is, to “list” species—and governs the activities that might affect listed species. Under the ESA, federal agencies must ensure that their actions do not harm listed species or jeopardize their existence. Accordingly, if EPA is deciding whether to register a pesticide, it must determine whether the action “may affect” a listed species. If the answer is yes, EPA has the option of initiating a formal consultation or conducting further analysis to determine whether the action is “likely to adversely affect” listed species. If EPA determines that the action is not likely to affect listed species adversely—and FWS or NMFS, as appropriate, agrees—no further consultation is required. However, if EPA determines that the action is likely to affect a listed species adversely, a formal consultation is required, and FWS or NMFS must determine whether the proposed action is likely to jeopardize the existence of the listed species. The product of that determination is called a biological opinion (BiOp) and is issued by FWS or NMFS.

Compliance with the ESA in registering pesticides creates some challenges. First, pesticides are intended to harm target organisms and are intentionally released into the environment. Other species that are in an area where a pesticide is applied could be exposed to and harmed by the pesticide. Second, FIFRA requires that EPA must determine before registering a pesticide that the use of the pesticide will not cause an unreasonable adverse effect on the environment, taking into account economic and social benefits associated with its use. That is, EPA weighs the costs to human health and the environment that could result from pesticide use against social and economic benefits, such as the benefits of mitigating disease vectors and reducing crop damage. The ESA prohibits jeopardizing listed species or adversely affecting their critical habitats but does not generally consider economic and social costs and benefits. Third, FIFRA creates a national registration process in which pesticides are registered on a nationwide basis, but the ESA calls for evaluating effects on specific species and their critical habitats and thus is geographically and temporally focused. The differences between the statutes have led to conflicting approaches in evaluating risks and have contributed to the current inability to reach consensus on assessing risks to listed species from pesticides.

A COMMON APPROACH

Compliance with the ESA in the context of pesticide registration requires EPA and the Services to determine the probability of adverse effects on listed species and their critical habitat when a pesticide is used according to its label requirements. Clearly, there are tensions among the agencies in making that de-

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termination, many of which seem to result from different assumptions, technical approaches (data and models used), and risk-calculation methods. What is needed is a common, scientifically credible approach that is acceptable to EPA and the Services. The committee concludes that the risk-assessment paradigm that traces its origins to the seminal NRC report *Risk Assessment in the Federal Government: Managing the Process*¹ and more recently to the NRC report *Science and Decisions: Advancing Risk Assessment*² provides such an approach. After 30 years of use and refinement, this risk-assessment paradigm has become scientifically credible, transparent, and consistent; can be reliably anticipated by all parties involved in decisions regarding pesticide use; and clearly articulates where scientific judgment is required and the bounds within which such judgment can be applied. The process is used for human-health and ecological risk assessments and is used broadly throughout the federal government. Thus, the committee concludes that the risk-assessment paradigm reflected in the ecological risk assessment (ERA) process is singularly appropriate for evaluating risks posed to ecological receptors, such as listed species, by chemical stressors, such as pesticides.

Figure S-1 shows the three major steps in the ESA process in connection with the ERA framework. As illustrated in the figure, the framework is the same at each step, but the contents of each element (problem formulation, exposure and effects analysis, and risk characterization) are expected to change as the focus shifts from assessing whether a pesticide "may affect" a listed species (Step 1) to whether it is "likely to adversely affect" a listed species (Step 2) to whether it is likely to jeopardize the continued existence of a listed species (Step 3). That is, the assessment becomes more focused and specific to the chemicals, species, and habitats of concern as it moves from Step 1 to Step 3. If the Services can build on the EPA assessment conducted for Steps 1 and 2 rather than conducting a completely new analysis for Step 3, the ERA will likely be more effective and scientifically credible. Although the committee does not expect the basic risk-assessment framework to change, it recognizes that risk-assessment approaches and methods for determining, for example, what is hazardous, what concentration or quantity is hazardous, what end points constitute an adverse effect, and when, where, and how much exposure is occurring will continue to evolve.

Given the changing scope of the ERA process from Step 1 to Step 3, EPA and the Services need to coordinate to ensure that their own technical needs are met. One approach is to use problem formulation, conducted as part of the ERA process, as an effective means for agencies to coordinate and reach agreement

¹NRC (National Research Council). 1983. *Risk Assessment in the Federal Government: Managing the Process*. Washington, DC: National Academy Press.

²NRC (National Research Council). 2009. *Science and Decisions: Advancing Risk Assessment*. Washington, DC: National Academies Press.

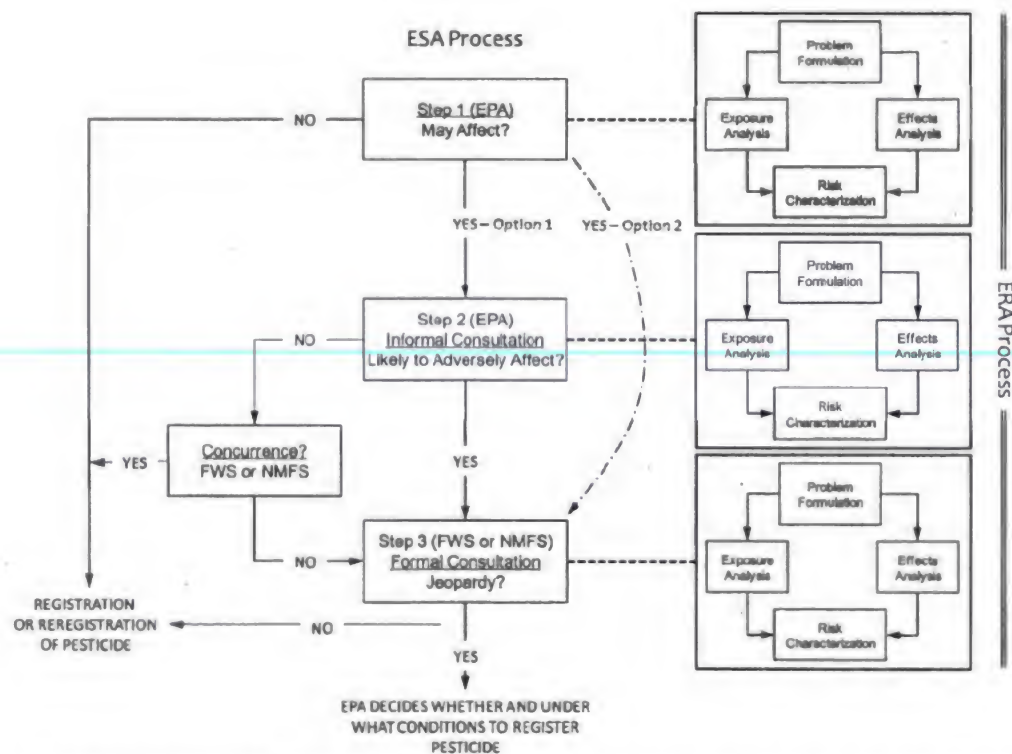


FIGURE S-1 Relationship between the Endangered Species Act (ESA) process and the ecological risk assessment (ERA) process. Each step answers the question that appears in the box.

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on many of the key technical issues involved in assessing risks posed to listed species by pesticides. Another approach would be to use technical working groups that address technical details of the assessment approach and other working groups to address policy-based issues. Regardless of the approach, the committee views coordination among EPA and the Services as a collegial exchange of technical and scientific information for the purpose of producing a complete and representative assessment of risk that includes a discussion on the types and depths of analyses needed for the decision and on the time and resources available.

BEST DATA AVAILABLE

One of the critical tasks in any risk assessment is to identify the data that will be used. The ESA directs the Services to conduct assessments on the basis of the "best scientific and commercial data available." However, the ESA, its legislative history, the rules and policies of the Services, and court cases contain little guidance for elaborating the meaning of that mandate, and the agencies do not appear to have formal protocols that define "best data available." Consequently, there have been some conflicts about what data to include in the assessments. EPA and the Services do have information-quality guidelines, and each appears to use assessment factors that include data-quality and data-relevance criteria.

Regardless of the breadth of the data collection, some guidelines—such as those listed below—need to be followed in identifying and selecting data for a credible assessment.

- *Document the strategy for all data searches and retrieval.* For example, if a repository database is searched, the date that the search was conducted and all search terms and search criteria should be documented. The content and scope of the repository, its criteria for inclusion and exclusion of data, the periodicity of its updates, and its quality-control measures also should be documented.
- *To ensure that the best data available are used, screen the data first for relevance.*³ Information that is not relevant clearly should not be used in assessing risk. Data should be from studies of the species and chemicals being assessed, or there should be a reasonable theoretical basis for data extrapolation. The data should also be applicable to the locations being considered and should be recent.
- *Review the quality of the relevant data before they are used in a risk assessment.*⁴ Sufficient information should be included to enable an independent

³Relevance refers to the applicability of the data for the intended purpose.

⁴Quality refers to the scientific adequacy of the design and execution of data collection, the analyses that use the data, and the data reporting.

evaluation of data quality. Data sources that lack sufficient details for adequate scientific evaluation—such as poster presentations, abstracts, anecdotal or personal communications, and secondary sources—might provide useful background knowledge or support an overall weight-of-evidence evaluation but should not be the sole basis of conclusions in an assessment.

- *For transparency, document the evaluation of all data used with particular attention to sources, relevance, and quality and describe any issues associated with those data attributes in the discussion of uncertainty in the risk characterization.*

Given that various stakeholders are aware of and can provide relevant and high-quality data, the committee encourages provision for their involvement in the early stages and throughout the risk-assessment process. The committee notes that stakeholder data are expected to meet the same standards of relevance and quality as all other data.

EXPOSURE

Exposure analysis is a principal component of ERA and involves estimating the concentrations of various chemicals released into the environment and their breakdown products of toxicological significance. The following sections discuss exposure-modeling practices and the criteria for authoritative geospatial data and highlight the committee's conclusions on those topics.

Exposure-Modeling Practices

To determine whether a pesticide will adversely affect or jeopardize the existence of a listed species or its critical habitat, one must estimate the concentration to which the species might be exposed or the concentration that might result in the ecosystem. To accomplish that task, chemical fate and transport models are used. Because the pathways by which pesticides move from their points of application to habitats of listed species can involve a complex sequence of transfers with diverse degradation processes, it is common to use a linked series of models to estimate exposure.

The committee acknowledges that the models used for exposure analyses have several strengths but emphasizes that a model's limitations need to be recognized and the model used in the appropriate context. As noted above, the committee has suggested a common approach that involves more refined and sophisticated modeling and analysis as one moves from Step 1 to Step 3 in the ESA process. Given the current practices in exposure analysis and the need to estimate pesticide exposures and the associated spatial-temporal variations experienced by listed species and their habitats, the committee envisions the following stepwise approach to exposure modeling.

- *Step 1 (EPA)*. Initial exposure modeling would answer the question, Do the areas where the pesticide will be used overlap spatially with the habitats of any listed species? The Services, which have extensive knowledge of the natural history of listed species, could help EPA to identify overlaps of areas where a pesticide might be used and the habitats of listed species.

- *Step 2 (EPA)*. If area overlaps are identified in Step 1, EPA would confer with the Services to identify relevant environmental compartments (water, soil, air, and biota), associated characteristics, and critical times or seasons in which environmental exposure concentrations need to be estimated. If the models indicate that substantial amounts of pesticides move off the application site and into the surrounding ecosystems, more sophisticated fate and transport processes could be used. At that point, the fate model could be simplified to remove processes that are unimportant in the specific regions where the listed species are and set up to estimate time-varying and space-varying pesticide concentrations in typical habitats with associated uncertainties. On the basis of the modeling results, EPA could then make a decision about the need for formal consultation with the Services.

- *Step 3 (Services)*. During a formal consultation, the Services would further refine the exposure models to develop quantitative estimates of pesticide concentrations and their associated distributions for the particular listed species and their habitats. To that end, the models would use site-specific input values, such as actual pesticide application rates, locally relevant geospatial data, and time-sensitive life stages of listed species.

The committee emphasizes that many parameters are used in chemical fate and transport models, and their accuracy is important ultimately to the concentrations estimated in the modeling efforts. Little effort has been expended in evaluating the data inputs relevant to particular ESA evaluations. Therefore, if the agencies want to obtain more accurate modeling results, a subset of case-specific exposure estimates should be evaluated by pursuing a measurement campaign specifically coordinated with several pesticide field applications. The committee notes that field studies need to be distinguished from general monitoring studies. General monitoring studies provide information on pesticide concentration on the basis of monitoring of specific locations at specific times and are not associated with specific applications of pesticides under well-described conditions. Therefore, general monitoring data cannot be used to estimate pesticide concentrations after a pesticide application or to evaluate the performance of fate and transport models.

Geospatial Data, Habitat Delineation, and Exposure Analysis

Habitat includes all environmental attributes present in an area that allow an organism to survive and reproduce, and habitat delineation is necessary for determining where a pesticide and a species might co-occur, for calculating spa-

tially explicit estimates of pesticide exposure, and for specifying the spatial structure of population models used in effects analysis (see below). Several methods for identifying and statistically modeling associations between species and their environment exist; although some caveats and uncertainties are associated with them, quantitative statistical habitat delineation is typically objective and more reliable than qualitative and subjective habitat descriptions.

The accuracy and reliability of habitat delineation and exposure analysis are increased substantially by the use of authoritative geospatial data. To be considered authoritative, geospatial data on any scale need to meet three criteria: availability from a widely recognized and respected source, public availability, and inclusion of metadata⁵ that are consistent with the standards of the National Spatial Data Infrastructure—a federal interagency program to organize and share spatial data and to ensure their accuracy. The geospatial data that are most useful for delineating habitat and estimating exposure are data on topography, hydrography, meteorology, solar radiation, soils, geology, and land cover. Table S-1 provides some examples of authoritative sources of those data. In many cases, there are multiple authoritative sources for each type of data on different spatial and temporal scales. Although it would be ideal to be able to identify specific authoritative sources, no one source will be best for all habitat delineations, exposure analyses, or other applications. However, accuracy assessments that generally are available for authoritative data sources might allow one to gauge which source is likely to be the most reliable for a particular objective.

EFFECTS

Pesticides are designed to have biological activity; specifically, they are “intended for preventing, destroying, repelling or mitigating” pests. Consequently, they have the potential to cause a variety of effects on nontarget organisms, including listed species. Determining the potential for and possible magnitude of effects is a process known as effects analysis. The following sections consider various topics on effects analysis as they are related to the committee’s task and highlight the committee’s conclusions on the topics.

Sublethal, Indirect, and Cumulative Effects

Pesticides can kill organisms but can also affect reproduction or growth or make organisms less competitive. Although EPA and the Services agree that those sublethal (less-than-lethal) effects should be considered in the assessment process, they disagree on the extent to which they can be included. To address

⁵Metadata document the fundamental attributes of data, such as who collected them, when and where they were collected, what variables were measured, how and in what units measurements were taken, and the coordinate system used to identify locations.

that issue, the committee first considered how to define objectively the degree to which observed effects are adverse. Defining adversity is essential for ERA because the mere existence of an effect is not sufficient to conclude that it is adverse. The committee concluded that the only way to determine whether an effect is adverse and how adverse it might be is to assess the degree to which it affects an organism's survival and reproductive success; any effect that results in a change in either survival or reproduction is relevant to the assessment, and any effect that does not change either outcome is irrelevant with respect to a quantitative assessment of population effects. Thus, EPA in Step 2 (see Figure S-1) should conduct a broad search to identify sublethal effects of pesticides and any information on concentration-response relationships. In Step 3, the Services should then show how such effects change probability of survival or reproduction of the listed species and incorporate such information into the population viability analyses or state that such relationships are unknown but possible and include a qualitative discussion in the uncertainty section of the BiOp. The inability to quantify the relationship between a sublethal effect and survival or reproductive success does not mean that the sublethal effect has no influence on population persistence; but in the absence of data, the relationship remains a hypothesis that can be discussed only qualitatively with reference to the scientific literature to explain why such a hypothesis is tenable.

TABLE S-1 Examples of Authoritative Sources of Geospatial Data

Data Type	Examples of Authoritative Data Sources
Topography	Topographic features can be derived from elevation data in the National Elevation Dataset, the Shuttle Radar Topography Mission, and the Global Digital Elevation Map.
Hydrography	Watershed data are available on line from EPA; watersheds are referred to by hydrologic unit codes of the US Department of Agriculture Natural Resources Conservation Service.
Meteorology	Data are available from the National Oceanographic and Atmospheric Administration National Climatic Data Center.
Solar radiation	Solar-radiation data are available from the National Aeronautics and Space Administration Earth Observing System Solar Radiation and Climate Experiment; ^a solar insolation can be estimated by using the on-line calculator of the Photovoltaic Education Network.
Soils	Soil surveys are available from the US Department of Agriculture Natural Resources Conservation Service.
Geology	Geological data are available from the US Geological Survey Mineral Resources Online Spatial Data.
Land cover	Land-cover data are available from the National Agricultural Statistics Service.

^aSolar-radiation measurements are taken at the top of Earth's atmosphere. Computer modeling is required to estimate solar radiation at Earth's surface.

In most cases, pesticides have the potential to affect a listed species indirectly—not through direct exposure but through effects on other species in the community. For example, the prey of a listed species might be reduced in abundance or eliminated by the pesticide, and this would affect the survival of the species. As in the case of sublethal effects, EPA and the Services differ about the degree to which indirect effects can be included in an assessment. The committee recommends that indirect effects that can be quantified relatively easily be incorporated into the effects analysis. However, determining and quantifying most indirect effects can be challenging and can require complex models. When such modeling is conducted, uncertainties should be estimated quantitatively in a realistic and scientifically defensible manner and should be propagated formally and explicitly through the analysis.

A risk assessor must also consider cumulative effects. They are defined by regulation under the ESA as “those effects of future State or private activities, not involving Federal activities that are reasonably certain to occur within the action area of the Federal action subject to consultation” (50 CFR 402.02). However, cumulative effects typically are more broadly defined as effects that interact or accumulate over time and space. The committee could not determine a scientific basis for excluding past and present conditions (the environmental baseline) from the consideration of cumulative effects and therefore used that broad definition in its evaluation. The committee concluded that population models provide a framework for incorporating baseline conditions and projected future cumulative effects into an effects analysis.

One problem that arises in an effects analysis is how to extrapolate toxicity information on tested species to listed species. Although the idea of identifying an appropriate surrogate species is appealing, the committee finds such identification problematic because different species often respond differently to chemical exposures, and the sensitivity differences can be large. Furthermore, different life histories can complicate the extrapolation. A scientifically defensible alternative approach is to define a range of sensitivities within which the sensitivity of a listed species could reasonably be expected to occur or a range of sensitivities that could be used to make reasoned extrapolations from information on species that have been tested by using inferences based on other chemicals. Further details are provided in Chapter 4 of this report.

Effects Models

EPA and the Services use different approaches to determine the potential effects of a pesticide on a listed species and its critical habitat. EPA addresses population effects simply as extensions of individual effects: if survival or reproduction is affected, EPA assumes population-level consequences and enters consultation with the Services. The Services use population models to address the question of population persistence explicitly. Population models are used to estimate population-level end points—such as population growth rate, probabil-

ity of population survival (population viability), and probability of population recovery—on the basis of individual-level effects. For purposes of population modeling, the effects must be estimated at a range of concentrations that includes all values that the populations being assessed might plausibly experience. Therefore, test results expressed only as threshold values, such as a no-observed-adverse-effect level or a lowest observed-adverse-effect level, are insufficient for a population-level risk assessment.

Because the ESA is concerned with species, ~~population models are necessary for quantifying the effects of pesticides on populations of listed species. Population models require three basic inputs: changes in survival or reproduction as a function of pesticide concentration, exposure estimates of pesticide concentration over time and space, and demographic and life-history information. There are a variety of population models, and the choice of a model will depend on the data available. Although species-specific models that incorporate all three inputs are preferred, in the absence of detailed demographic information it is reasonable to use simple generic models that characterize the life history of a group of species to estimate the effects of a pesticide on a given species. It is important to incorporate density dependence by using models with parameter values that are functions of population density or population size, but it is not accurate to assume that mortality due to pesticide exposure will be compensated for by density dependence because it is likely that such exposure will decrease the growth rate of the population at all densities and generally depress the curve of population size vs growth rate.~~

MIXTURES: AN IMPORTANT CONCERN FOR EXPOSURE AND EFFECTS ANALYSIS

Assessing the risks posed by exposure to mixtures is clearly a subject of disagreement and concern for the agencies. To address the mixture issue, the committee made several distinctions. First, some pesticides might contain more than one active ingredient (a chemical that is responsible for the biological effect of the pesticide); most pesticides contain other chemicals that are typically designated as "inerts."⁶ Second, pesticides are often mixed with other chemicals before their application. The resulting mixtures are referred to as tank mixture and can contain other pesticides, fertilizers, and adjuvants—materials that facilitate handling and application, such as surfactants, compatibility agents, anti-foaming agents, and drift-control agents. Third, chemicals from other sources are already in the environment; unless exposure occurs only at or near the point of pesticide application, species are more likely to be exposed to environmental mixtures than to a single pesticide formulation or tank mixture. Environmental

⁶The term *inerts* is defined by FIFRA as an ingredient that is not active. Inerts are intentionally added to pesticide products, and the term does not mean that the chemicals are nontoxic.

mixtures are formed when a tank mixture—active ingredients, inerts, and adjuvants—combines with other chemicals in the environment from other sources. Ideally, assessments should be based on exposure to all pesticide components and to other chemicals that are present in the exposure environment. However, quantitative estimates of exposure to environmental mixtures are difficult given the dynamic state of environmental mixtures over space and time. In any given location, the amounts of pesticide active ingredients, inerts, adjuvants, and other environmental chemicals are highly variable and depend on pesticide uses and other sources of environmental contamination.

EPA recognizes the potential importance of exposure to mixtures but typically assesses only pesticide active ingredients. The Services have expressed substantial concern about the need to account for mixture exposure but have dealt with the issue only with a qualitative discussion in their assessments. The greatest concern is that a mixture component might act to enhance the toxicity of a pesticide active ingredient. The committee notes that a quantitative assessment of the risk posed by chemical mixtures requires extensive data, including data on the identity, concentration, and toxicity of mixture components. Challenges in assessing risk to listed species posed by pesticide-containing mixtures arise largely because of the lack of such data *and* the lack of understanding of the potential for interactions among mixture components. In the absence of such quantitative data, the possible contribution of specific mixture components to the toxicity of a pesticide active ingredient cannot be incorporated into a quantitative risk assessment. The committee, however, emphasizes that the complexity of assessing the risk posed by chemical mixtures should not paralyze the process, and it provides guidelines in Chapter 4 of its report to help in determining when and how to consider components other than a pesticide active ingredient in a risk assessment.

RISK CHARACTERIZATION AND UNCERTAINTY

Risk characterization is the final stage of a risk assessment in which the results of the exposure and effects analyses are integrated to provide decision-makers with a risk estimate and its associated uncertainty. Two general approaches have been used for risk characterization: the risk-quotient (RQ) approach, which compares point estimates of exposure and effect values, and the probabilistic approach, which evaluates the probability that exposure to a chemical will lead to a specified adverse effect at some future time.

The RQ approach does not estimate risk—the probability of an adverse effect—itself but rather relies on there being a large margin between a point estimate that is derived to maximize a pesticide's environmental concentration and a point estimate that is derived to minimize the concentration at which a specified adverse effect is not expected. If the results raise doubts regarding the possibility of an adverse effect, the common response is to widen the margin by, for example, adding uncertainty factors or assuming more stringent, and possibly

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implausible, exposure scenarios. The flaw in that approach is that there is no accounting for what the probability of an adverse effect was before the application of assumptions, and there is no calculation of how their use modifies that probability. Accordingly, the committee concludes that adding uncertainty factors to RQs to account for lack of data (on formulation toxicity, synergy, additivity, or any other aspect) is unwarranted because there is no way to determine whether the assumptions that are used overestimate or underestimate the probability of adverse effects. Furthermore, the committee concludes that RQs are not scientifically defensible for assessing the risks to listed species posed by pesticides or indeed for any application in which the desire is to base a decision on the probabilities of various possible outcomes.

Instead, the committee recommends using a probabilistic approach that requires integration of the uncertainties (from sampling, natural variability, lack of knowledge, and measurement and model error) into the exposure and effects analyses by using probability distributions rather than single point estimates for uncertain quantities. The distributions are integrated mathematically to calculate the risk as a probability and the associated uncertainty in that estimate. Ultimately, decision-makers are provided with a risk estimate that reflects the probability of exposure to a range of pesticide concentrations and the magnitude of an adverse effect (if any) resulting from such exposure.

The committee recognizes the pragmatic demands of the pesticide-registration process and encourages EPA and the Services to consider the probabilistic methods that have already been successfully applied to pesticide risk assessments, that have otherwise appeared often in the technical literature, that are familiar to many risk-assessment practitioners, that can be implemented with commercially available software, and that are most readily explicable to decision-makers, stakeholders, and the public. The committee also recognizes that administrative and other nonscientific hurdles will need to be overcome to implement this approach, but moving the uncertainty analysis from the typical narrative addendum to an integral part of the assessment is possible and necessary to provide realistic, objective estimates of risk.

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Introduction

The US Endangered Species Act (ESA) requires federal agencies to consult with the Fish and Wildlife Service (FWS) or the National Marine Fisheries Service (NMFS) when a federal action might affect a species that is listed as threatened or endangered (that is, a listed species) or its designated critical habitat. One such action that could potentially affect listed species or their critical habitats is the registration (or reregistration) of pesticides by the US Environmental Protection Agency (EPA) under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Accordingly, EPA must first determine whether the registration (or reregistration) of a pesticide “may affect” a listed species. If so, EPA must initiate formal consultation *or* determine whether it is “likely to adversely affect” a listed species. If EPA determines that the pesticide registration is “not likely to adversely affect” a listed species—and FWS or NMFS, as appropriate, agrees—no further consultation is required. However, if EPA determines that the pesticide registration is “likely to adversely affect” a listed species, a formal consultation is required, and the product of that formal consultation is a biological opinion (BiOp) issued by FWS or NMFS. Over the last decade, several court cases have made it clear that formal or informal consultation is required when EPA registers or reregisters a pesticide that might affect a listed species. The consultations that have resulted from the court cases raise questions regarding the best approaches or methods for determining risks to listed species and their critical habitats. Because EPA, FWS, and NMFS have some fundamental differences in approaches, they and the US Department of Agriculture (USDA) asked the National Research Council (NRC) to examine scientific and technical issues related to determining risks to ESA-listed species from pesticides that are registered under FIFRA. As a result of the request, NRC convened the Committee on Ecological Risk Assessment under FIFRA and ESA, which prepared the present report.

THE FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT

FIFRA is the federal statute that governs the sale, distribution, and use of pesticides in the United States [7 U.S.C. §§ 136-136y]. EPA has the primary

responsibility for administering FIFRA, and the states play an important role in enforcing the act. Under FIFRA, the term *pesticide* is defined as "any substance or mixture of substances intended for preventing, destroying, repelling or mitigating any pest" [7 U.S.C. § 136 (u)(1)].

Pursuant to FIFRA Section 3(a), a pesticide may not be sold or distributed in the United States without a license, known as a registration, from EPA. To obtain a FIFRA registration, an applicant must demonstrate, among other things, that the pesticide will "perform its intended function without unreasonable adverse effects on the environment" [§ 136a (c)(5)(C)] and that when the pesticide is "used in accordance with widespread and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment" [§ 136a (c)(5)(D)]. FIFRA defines *environment* as "water, air, land, and all plants and man and other animals living therein and the interrelationships which exist among these" [§ 136 (j)]. It defines the phrase *unreasonable adverse effects on the environment* as any "unreasonable risk to man or the environment taking into account the economic, social, and environmental costs and benefits of the use of any pesticide" [§ 136 (z)(bb)(1)]. In other words, when deciding whether a particular pesticide meets the standard for registration, EPA must consider the economic and social benefits of using the pesticide and the risks to humans and the environment posed by its use. EPA has interpreted the "unreasonable adverse effects on the environment" standard to require a balancing of costs and benefits in which EPA weighs the costs to human health and the environment resulting from pesticide use against social and economic benefits, such as the benefits of mitigating disease vectors and reducing crop damage.

To obtain a registration, an applicant must provide data demonstrating that its pesticide does not cause unreasonable adverse effects. FIFRA does not mandate that any particular tests be conducted or that any particular type of data be submitted to obtain a registration. However, FIFRA Section 3(c)(2)(A) directs EPA to publish guidelines "specifying the kinds of information which will be required to support the registration of a pesticide" and directs EPA to revisit and revise these guidelines "from time to time." Pursuant to that section, EPA has promulgated rules in 40 C.F.R. Part 158 that establish data requirements for demonstrating that a particular pesticide product meets the standard for registration. Excerpts from Part 158 are provided in Appendix A of the present report. EPA has also developed a series of test guidelines that specify methods for conducting the studies that will generate the data to support registration.

Many of the data requirements in Part 158 address general information about a pesticide, such as its chemical composition and chemical and physical properties. Other data requirements focus on mammalian testing that can be used to evaluate the human health effects of pesticide exposure. Most important for purposes of this report, Part 158 includes a number of sections related to environmental risk, including risks to species that are not the targets of the pesticide (that is, nontarget species). For example, Subpart G requires avian oral toxicity testing, avian dietary toxicity testing, and avian reproduction testing and might require wild-mammal toxicity testing and simulated or actual field testing. Addi-

tional data on wildlife are required only case by case. Subpart G also requires acute toxicity tests on honeybees and various toxicity tests on freshwater fishes, freshwater invertebrates, and estuarine and marine organisms. Subpart L sets forth requirements for spray-drift data, and Subpart N sets forth requirements for environmental fate data, which are targeted at assessing "the presence of widely distributed and persistent pesticides in the environment which may result in loss of usable land, surface water, ground water, and wildlife resources, and...the potential environmental exposure of other nontarget organisms, such as fish and wildlife, to pesticides" [40 C.F.R. § 158.130(h)(1)].

If, after evaluating the data submitted, EPA determines that the applicant has demonstrated that the standard for registration has been met, it will issue a registration. The registration will specify use restrictions that EPA has determined are necessary to meet the standard for registration. Most important, the registration will require that the pesticide be labeled with specific product information, directions for use, and hazard information. The product label dictates legal use of the pesticide. FIFRA provides that it is a violation of federal law "to use any registered pesticide in a manner inconsistent with its labeling" [§ 136 (j)(a)(2)(G)], and every registered pesticide product is required to bear a label containing this warning. Accordingly, the label is the vehicle not only for providing important information to end users but for mandating the purposes for which and the manner in which end users may use the pesticide product. The label instructions are necessary to ensure that the pesticide meets the standard for registration. A pesticide that might have an unreasonable adverse effect on the environment if used at a particular dosage, for a particular crop type, or in a particular manner might not have an unreasonable adverse effect if its use is restricted to other specified crops or specified application rates or restricted in other ways to minimize human health or environmental risks. Thus, the label language is EPA's primary regulatory tool for reducing pesticide risk under FIFRA. Users who fail to comply with label directions can incur penalties, although in practice it is extremely difficult to monitor every pesticide application to determine whether it was carried out according to the label.

Once a pesticide is registered, EPA does not require a permit or any other approvals before it is used. That is, there is no evaluation of specific pesticide applications; thus, the geographic and temporal factors specific to an application site or timing are not evaluated before the pesticide is released into the environment. However, some states have their own pesticide-permitting programs that apply to specific types of pesticide use (for example, aerial application). Furthermore, EPA has the authority under FIFRA to classify specific pesticides as "restricted use pesticides." Those pesticides can be used only under the supervision of a certified applicator who has received training in the proper handling and use of the pesticide in question. However, even when there are state permitting requirements and certified-applicator-training requirements, most pesticide use is regulated only by label restrictions without a requirement for a permit or other approval before use.

After a pesticide product is registered, FIFRA continues to impose responsibilities on the registrant, and EPA can require additional data submission. FIFRA Section 6(a)(2) requires that if at any time after the issuance of a registration a registrant obtains information that a pesticide has unreasonable adverse effects on the environment, the registrant is required to submit the information to EPA. And FIFRA Section 3(c)(2)(B) states that "if [EPA] determines that additional data are required to maintain in effect an existing registration of a pesticide, [EPA] shall notify all existing registrants of the pesticide to which the determination relates." If EPA invokes Section 3(c)(2)(B), referred to as a "data call-in," each registrant must provide evidence to EPA within 90 days that it is "taking steps to secure the additional data required." If EPA determines that a registrant has failed to take appropriate steps to secure the required data, it may initiate proceedings to suspend the registration of the pesticide. EPA can cancel a registration if it determines that a pesticide or its labeling does not comply with FIFRA or if the pesticide "generally causes unreasonable adverse effects on the environment when used in accordance with widespread and commonly recognized practice" (75 Fed. Reg. 68297[2010]). FIFRA Section 6(c) authorizes the suspension of a registration if EPA determines that suspension is necessary to prevent an imminent hazard during the time required for cancellation. FIFRA Section 2(l) defines *imminent hazard* to include a "situation which exists when the continued use of a pesticide during the time required for cancellation proceeding...will involve unreasonable hazard to the survival of a species declared endangered or threatened by the Secretary pursuant to the Endangered Species Act of 1973."

Congress has on several occasions directed EPA to review the human health and environmental effects of pesticides registered before some specified date. In 1972, revisions of FIFRA mandated that EPA re-evaluate registered pesticides—a process known as reregistration—by using current scientific and regulatory standards to ensure that the data used to register the pesticides originally meet current standards. In 1988, Congress imposed specific reregistration requirements that were intended to improve the speed and the nature of reregistration. The 1988 provisions established a multistep process with various deadlines intended to ensure that registrants submit required data to EPA in a timely manner. Under the 1988 amendments, failure to meet the data-submission deadlines could result in suspension or cancellation of a registration.

In 1996, Congress passed the Food Quality Protection Act (FQPA), which also amended FIFRA. The FQPA was focused on providing additional protections for humans, not wildlife, and required EPA to re-evaluate many food-use pesticides under new human-health standards. As a result of the re-evaluation, EPA canceled some pesticide uses, changed allowable application rates, and imposed use restrictions on others that were not aimed at reducing risk to wildlife but had that result.

THE ENDANGERED SPECIES ACT

The ESA is the federal statute that creates the authority to designate species as threatened or endangered and governs the activities that might affect those species (Endangered Species Act 16 U.S.C. §§ 1531–1544). The ESA is administered and enforced by two federal agencies that have jurisdiction for species in different ecosystems. FWS, in the Department of the Interior, typically is responsible for freshwater and terrestrial species, and NMFS, in the Department of Commerce, typically is responsible for marine and anadromous species (species that migrate from marine to freshwater environments to spawn, such as Pacific salmonids). The two agencies—referred to collectively as the Services and individually as the Service—are responsible for listing species as endangered or threatened under the ESA.

An *endangered species* is defined as a “species which is in danger of extinction throughout all or a significant portion of its range” [16 U.S.C. § 1532 (6)]. A *threatened species* is defined as a species that is “likely to become...endangered...within the foreseeable future throughout all or a significant portion of its range” [§ 1532 (20)]. Subspecies of “fish or wildlife or plants and any distinct population segment of any species of vertebrate fish or wildlife which interbreeds when mature” [§ 1532 (16)] are also included in the ESA’s definition of species and thus can be listed. In this report, the terms *endangered species*, *threatened species*, and *listed species* can refer to subspecies or distinct population segments as defined by the ESA. Once a species is listed, the ESA requires that the Services designate critical habitat for each listed species. As of October 15, 2012, critical habitat had been designated for 653 of the 1,434 listed species that occur in the United States.

Endangered species are subject to several protections under the ESA, and threatened species are for the most part subject to the same protections. ESA Section 9 prohibits the “take” of listed species. The statute defines *take* as “harass, harm, pursue, hunt, shoot, wound, kill, trap, capture, or collect or attempt to engage in any such conduct” [16 U.S.C. § 1532 (19)]. The Services have further defined *harm* to include acts that involve substantial habitat modification or degradation that kills or injures listed species by substantially impairing essential behavior patterns, including breeding, feeding, and sheltering. That broad interpretation of harm has been upheld by the US Supreme Court [*Babbitt v Sweet Home Chapter of Communities for a Greater Oregon*, 515 U.S. 687, 698 (1995)]. The ESA authorizes the Services to assess penalties for unauthorized take of listed species and authorizes courts to impose injunctions to prevent a take from occurring or continuing. A federal agency (such as EPA) is liable for its actions, including, at least according to one court, the issuance of FIFRA registrations that result in a take of a listed species [*Defenders of Wildlife v Administrator, EPA*, 882 F. 2d 1294 (8th Cir. 1989)].

Section 7 of the ESA includes another important provision that specifically applies to actions of federal agencies. It mandates that federal agencies use their existing authorities to conserve endangered and threatened species and

consult with the Services to ensure "that any action authorized, funded, or carried out by such agency is not likely to jeopardize the continued existence of any endangered species or threatened species or result in the destruction or adverse modification of [critical habitat] of such species" [16 U.S.C. § 1536 (a)(2)]. The phrase "jeopardize the continued existence of [a listed species]" means "to engage in an action that reasonably would be expected, directly or indirectly, to reduce appreciably the likelihood of both the survival and recovery of a listed species in the wild by reducing the reproduction, numbers, or distribution of that species" [50 CFR § 402.02].

Any proposed federal agency action that "may affect" listed species is subject to ESA Section 7 and could require a formal consultation (see Figure 1-1). The term "may affect" is defined broadly to include beneficial and adverse effects. For any action that "may affect" listed species, the action agency has two options: it may choose to initiate formal consultation or may determine whether the action is "likely to adversely affect" listed species. If the action agency determines, with written concurrence of FWS or NMFS, that the action is "not likely to adversely affect" a listed species or its critical habitat, no further consultation is required. However, if the action agency determines that the action is "likely to adversely affect" a listed species or its critical habitat, formal consultation is required. Through the formal consultation process, FWS or NMFS determines whether the proposed federal agency action is likely to jeopardize listed species; if so, FWS or NMFS will develop "reasonable and prudent alternatives" (RPAs) that, if implemented, are expected to avoid jeopardy. It is at the action agency's discretion whether to adopt the RPAs. However, the agency will be liable under Section 9 if a take results from its action and the take was not provided for by an incidental take statement (ITS) in the BiOp, the final document issued by FWS or NMFS. An ITS describes actions that will not be considered prohibited takes and describes "reasonable and prudent measures" that must be complied with to be covered by the ITS.

Unlike FIFRA and its implementing regulations, the ESA does not prescribe specific studies that must be conducted or specific data that must be collected or submitted in the consultation process. Instead, in several provisions of the ESA, Congress has directed the Services to make determinations based on the "best scientific and commercial data available." Similarly, the Services' rules on consultation state that

the Federal agency requesting formal consultation shall provide the Service with the best scientific and commercial data available or which can be obtained during the consultation for an adequate review of the effects that an action may have upon listed species or critical habitat. This information may include the results of studies or surveys conducted by the Federal agency or the designated non-Federal representative. The Federal agency shall provide any applicant with the opportunity to submit information for consideration during the consultation [50 C.F.R. 402.14(d)].

In formulating its biological opinion, any reasonable and prudent alternatives, and any reasonable and prudent measures, the Service will use the best scientific and commercial data available [50 C.F.R. 402.14(g)(8)].

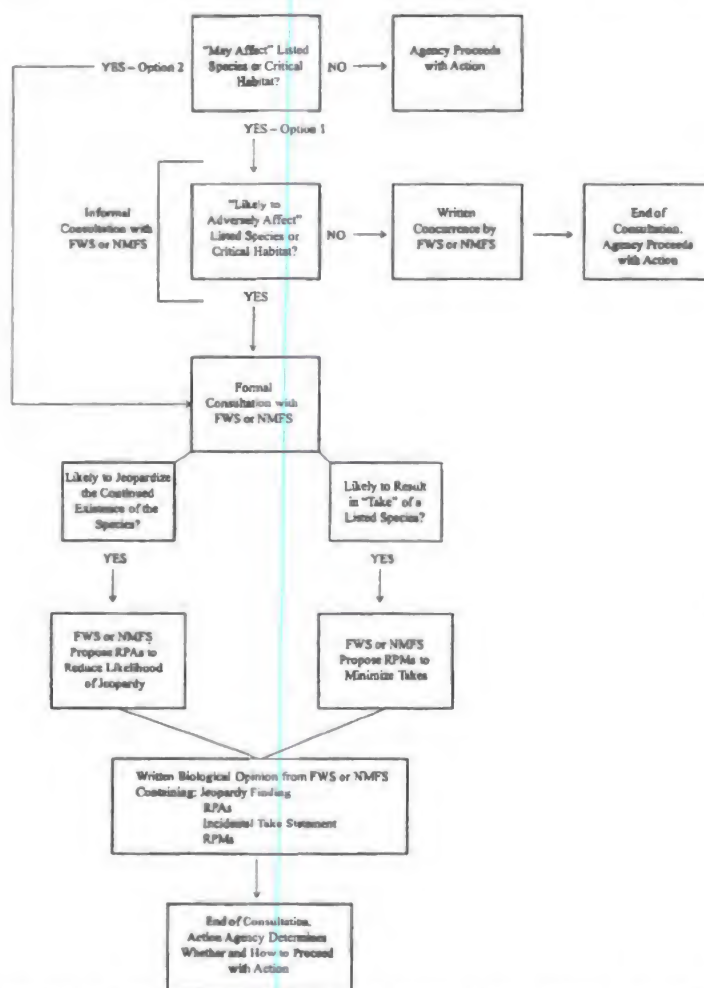


FIGURE 1-1 Consultation process under ESA Section 7 for a federal action that potentially could affect a listed species or critical habitat. If the agency determines that the action "may affect" the listed species or critical habitat, it has two options: (1) determine whether the action is "likely to adversely affect" or (2) go directly to formal consultation with the appropriate Service. Abbreviations: FWS, Fish and Wildlife Service; NMFS, National Marine Fisheries Service; RPA, Reasonable and Prudent Action; RPM, Reasonable and Prudent Measure.

The Services have also issued two policy statements on implementing the “best scientific and commercial data available” mandate. The first is the *Notice of Interagency Cooperative Policy on Information Standards* [59 Fed. Reg. 34271 (July 1, 1994)]. It applies to, among other things, decisions made in the Section 7 consultation process and states that biologists employed by the Services must evaluate all information to “ensure that any information used by the Services to implement the Act is reliable, credible, and represents the best scientific and commercial data available.” It also expresses a preference that the Services use primary and original sources of information as the basis of its recommendations.

The second policy statement is the *Notice of Interagency Cooperative Policy for Peer Review in Endangered Species Act Activities* [59 Fed. Reg. 3270 (July 1, 1994)]. It provides that in making listing decisions and developing recovery plans under the ESA, the Services will seek independent peer review. It does not explicitly apply to decisions made in the Section 7 consultation process.

Neither the ESA nor its implementing regulations or policies provide detailed guidance on what is meant by “best scientific and commercial data available.” Moreover, the legislative history of the ESA does not provide any clear direction on what Congress intended by using that language. However, experts who have studied the ESA, its legislative history, and circumstances surrounding the passage of the act have stated that the “best scientific and commercial data” mandate was generally intended to “ensure objective, value-neutral decision making by specially trained experts” (Doremus 2004). As one expert has opined, “taking the best available science mandate at face value, its most obvious purpose would seem to be to ensure that agency decisions are substantially as ‘good’ as can be” (Doremus 2004). Experts who have analyzed the case law involving the use of the best-available-science mandate have concluded that the cases suggest “no consistent thread or logic” (Brennan et al. 2003). Thus, there is little guidance in the ESA, its legislative history, the Services’ rules and policies, or court cases to elaborate the meaning of the “best scientific and commercial data available” mandate in the ESA.

THE RELATIONSHIP BETWEEN THE TWO ACTS

At least one court has held that EPA can be liable for a take under the ESA if its registration of a pesticide results in the take of a listed species [*Defenders of Wildlife v Administrator, EPA*, 882 F. 2d 1294 (8th Cir. 1989)]. More important for the purposes of the present report, courts have held that EPA is required to comply with the ESA Section 7 consultation process when registering or taking other regulatory actions on pesticides under FIFRA. The requirement that EPA comply with the ESA when registering pesticides under FIFRA presents a number of challenges. First, pesticides, by their very nature, are intended to harm or disrupt a living organism in some way. Pesticides intended for out-

door agriculture, forestry, weed control, and other uses are also intentionally released into the environment. Consequently, if any listed species nest, roost, migrate through, or otherwise exist in a particular geographic location where pesticides are released, they could be exposed to potentially harmful substances, and takes could occur.

As described above, the ESA prohibits any take of a listed species and requires formal consultation for any agency action that is likely to affect any listed species adversely. FIFRA, in contrast, requires a cost-benefit balancing of the risks associated with the use of a pesticide and the social and economic benefits to be gained by its use. The ESA prohibits takes of listed species and seeks to ensure that federal agency actions do not jeopardize the continued existence of a listed species. Economic considerations do not come into play in ESA listing, take, or jeopardy evaluations as they do under FIFRA. The FIFRA cost-benefit standard applies whether or not listed species are at issue, although presumably harm to a listed species would be considered a high cost. In fact, the only place where FIFRA mentions threatened or endangered species is in Section 6(c)(1) of FIFRA, which authorizes EPA to "suspend the registration of a pesticide [if that] is necessary to prevent an imminent hazard during the time required for a cancellation proceeding." As noted above, FIFRA Section 2(l) defines *imminent hazard* to include a "situation which exists when the continued use of a pesticide during the time required for cancellation proceeding . . . will involve unreasonable hazard to the survival of a species declared endangered or threatened." FIFRA does not provide EPA with any other direction concerning listed species.

Another challenge for EPA in complying with the ESA for pesticide registrations is that FIFRA creates a national registration process whereas the ESA requires an evaluation of effects on the habitat of a listed species and individual members of a species. Under FIFRA, pesticide registration or cancellation decisions are made on a nationwide basis. The ESA, in contrast, is geographically and temporally focused. Although EPA typically considers geographic fate and exposure scenarios relevant to where and when a pesticide is expected to be used, it is challenging to design label restrictions and warnings to ensure that there is never an effect on a listed species.

Another difference between FIFRA and the ESA concerns data available for assessments. As indicated above, FIFRA requires the submission of data before registration, whereas under the ESA the Services are mandated to rely on the best data available (as opposed to requesting new data). Furthermore, under the ESA, decisions are not to be delayed because of a lack of data.

The differences between the statutes have led EPA and the Services to develop different approaches to ecological risk assessment that have often made it difficult for them to reach a scientific agreement. As a result, EPA and the Services decided to seek advice from the NRC on several scientific issues related to conducting an ecological risk assessment.

THE COMMITTEE AND ITS TASK

The committee that was convened in response to the request from EPA, FWS, NMFS, and USDA included experts on salmonid biology, ecology, hydrology, geospatial analysis, exposure analysis, toxicology, population dynamics, statistics, uncertainty analysis, environmental law, and ecological, pesticide, and mixture risk assessment (see Appendix B for biographical information). The committee was asked to evaluate EPA's and the Services' methods for determining risks to listed species posed by pesticides and to answer questions concerning the identification of the best scientific data, the toxicological effects of pesticides and chemical mixtures, the approaches and assumptions used in various models, the analysis of uncertainty, and the use of geospatial data. See Box 1-1 for a verbatim statement of the committee's task.

THE COMMITTEE'S APPROACH TO ITS TASK

The committee held five meetings to assist it in accomplishing its task. The first three included open sessions during which the committee heard from the sponsors and invited speakers from academe, professional organizations, nonprofit organizations, and consulting agencies. The committee submitted written questions to the sponsors to clarify the charge questions, discussed their responses in an open session, and reviewed extensive literature on various aspects of ecological risk assessment and materials provided by the sponsors and stakeholders. As directed in its statement of task, the committee used the recent consultations between the NMFS and EPA as a reference for its evaluation of assessment methods used by EPA and the Services. It emphasizes that it did not specifically evaluate the biological opinions or EPA's effect determinations on Pacific salmonids; that would have been outside its charge. For ease of discussion, the committee has designated the steps in the ESA process—"may affect," "likely to adversely affect," and "likely to jeopardize"—as Steps 1, 2, and 3 in this report.

The committee does not take a position on any legal or regulatory policy issue, provide any legal or policy advice, or comment on the merit of any particular court ruling or other legal or policy decision. Furthermore, it recognizes that the agencies must make regulatory policy choices, and it has consciously avoided commenting on regulatory policy. In fact, the committee concludes that science and regulatory policy need to be kept separate to the extent possible and that there should be transparency where policy is involved. The present report evaluates the science of ecological risk assessment. Once an assessment is conducted, the involved agencies are responsible for making policy decisions pursuant to their legal mandates. The committee uses the generic term *decision-maker* to indicate a person who will use the results of a risk assessment to inform a decision. The committee makes no statements on who such a person should be; that is a policy issue.

BOX 1-1 Statement of Task

A committee of the National Research Council (NRC) will examine scientific and technical issues related to the methods and assumptions used by the U.S. Environmental Protection Agency (EPA), the U.S. Fish and Wildlife Service (FWS), and the National Oceanic and Atmospheric Administration (NOAA) to conduct scientific assessments of ecological risks from pesticides registered by EPA under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) to species listed under the Endangered Species Act (ESA). The range of scientific studies needed to make such assessments will be considered, including ecological, hydrological, toxicological, and exposure studies. The committee will develop conclusions reflecting the use of scientific principles and to facilitate a more holistic approach to assessing risks across the agencies, considering the intent of the ESA and of FIFRA. Policy issues related to decision making will not be addressed. Specific topics that the committee will consider to the extent practicable include the following:

- **Best available scientific data and information.** The Services and EPA approach the identification of "best available scientific information" using a variety of differing protocols pertaining to the type and character of scientific information that may be appropriate for these evaluations. Some of these approaches pertain to the character of the information as consensus information, peer-reviewed information, regulatory studies supporting pesticide registrations, or other published and unpublished information. The NRC will evaluate those protocols with respect to validity, availability, consistency, clarity, and utility.
- **Sublethal, indirect, and cumulative effects.** The ESA requires the consideration of direct, indirect, and cumulative effects on listed species and habitats in the consultation process. The Services and EPA have used differing approaches on how to characterize indirect, sub-lethal, and cumulative effects. The NRC will review the best available scientific methods for projecting these types of effects and consider options for the development of any additional methods that are likely to be helpful.
- **Mixtures and inerts.** Assessing the effects of the use of chemical mixtures, either in formulated products or as used at the field level, remains a complex and difficult challenge, as is assessing the effects of mixtures of pesticides and other environmental contaminants. Projecting the effects of inert ingredients such as adjuvants, surfactants, and other pesticide product additives is also an area of continuing challenge. The NRC will consider the scientific information available to assess the potential effects of mixtures and inert ingredients.
- **Models.** There is a range of approaches to the development and use of modeling to assist in analyzing the effects of actions such as using pesticides or alternatives to that use, and active issues remain about the use of unpublished models or the assumptions used in the choice of the available models for any particular analysis of effects. The NRC will assess the protocols governing the development of assumptions associated with model inputs and the use of sensitivity analyses to evaluate the impact of multiple assumptions on the interpretation of model results.

- **Interpretation of uncertainty.** There are a variety of methods for documenting and interpreting uncertainties and evaluating the extent to which uncertainties impact confidence in the scientific conclusions associated with a jeopardy decision. In particular, the NRC will consider the selection and use of uncertainty factors to account for lack of data on formulation toxicity, synergy, additivity, etc., and how the choice of those factors affects the estimates of uncertainty.

- **Geospatial information and datasets.** Location of the habitat is an important component of successfully protecting the impacted species. Much variability in datasets, geospatial layers, and scale contributes to uncertainty. The NRC will consider what constitutes authoritative geospatial information, including spatial and temporal scale that most appropriately delineates habitat of the species and the duration of potential effects.

In its deliberations, the NRC will focus on the scientific and technical methods and approaches the agencies use in determining risks to endangered and threatened species associated with the use of pesticides. The NRC will provide conclusions as appropriate about techniques the agencies might apply or use to improve those methods and approaches using scientific principles to support their decision-making.

As examples, the NRC will consider three recent consultations between NOAA and EPA on the effects of EPA's proposed FIFRA actions on Pacific salmonids as reference points for its work. The NRC will use the consultations as examples of the various agencies' scientific approaches and methods but will not evaluate the consultations themselves or the decisions resulting from them, and it will not limit its considerations strictly to aquatic species.

ORGANIZATION OF THE REPORT

The committee's report is organized into five chapters. Chapter 2 presents a common approach to the assessment process and discusses some overarching issues regarding uncertainty and best data available. Chapters 3 and 4 focus on exposure and effects analysis, respectively; each describes models and issues associated with uncertainty. Chapter 5 addresses the risk characterization process, which combines the results of the exposure and effects analyses. Excerpts of CFR Part 158 are provided in Appendix A, and Appendix B presents biographical information on the committee.

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- Doremus, H. 2004. The purposes, effects, and future of the Endangered Species Act's best available science mandate. *Environ. Law* 34:397-450.

2

A Common Approach and Other Overarching Issues

The committee was asked to comment specifically on scientific and technical approaches that might assist the US Environmental Protection Agency (EPA), the National Marine Fisheries Service (NMFS), and the Fish and Wildlife Service (FWS) in estimating risk to species listed under the Endangered Species Act (ESA) posed by pesticides (chemical stressors) under review by EPA for registration or reregistration as required by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). In this chapter, the committee discusses how the risk-assessment paradigm could serve as a common approach for EPA and the Services (NMFS and FWS) in examining the potential for listed species to be exposed to pesticides and the probability (that is, the risk) that such exposures would result in adverse effects. The risk-assessment paradigm was originally set forth in the report *Risk Assessment in the Federal Government: Managing the Process* (NRC 1983) and has been used and refined over the last few decades to evaluate both human health and environmental risks. Because this report is focused on risk to listed species in the environment posed by pesticide exposure, the committee focuses on ecological risk assessment (ERA) as described by such comprehensive references as Suter (2007). This chapter also addresses two general issues related to risk assessment: analysis of uncertainty and use of best data available.

A COMMON APPROACH

To comply with or administer the ESA during the pesticide registration process, EPA and the Services need to determine the probability of adverse effects on listed species or their habitats due to expected pesticide use that is consistent with label requirements. The committee understands that EPA and the Services are responding to different federal regulations and legal requirements

and that the ESA places different responsibilities on the action agency (EPA) and the decision agency (NMFS or FWS). However, the committee has concluded that when the determination involves risk posed by chemical stressors, the agencies should use the same ERA paradigm to reach conclusions about adverse effects. Scientific obstacles to reaching agreement between EPA and the Services during consultation have emerged apparently because of the agencies' differences in implementation of the ERA process, including differences in underlying assumptions, technical approaches, data use, exposure models, and risk-calculation methods. Agreement has also been impeded because of a lack of communication and coordination throughout the process.

To understand and reconcile the differences between how EPA assesses risk to listed species from pesticide use and how the Services reach jeopardy decisions, it is important first to understand the consultation process under the ESA. The Services' *Endangered Species Consultation Handbook* (FWS/NMFS 1998) details the procedural and legal steps that they must follow when engaging in informal or formal consultations regarding listed species. As discussed in Chapter 1, the process involves three steps; the first two steps are to determine whether a proposed action needs formal consultation (Figure 2-1). In Step 1, the action agency (EPA) determines whether the action "may affect" a listed species. If the answer is yes (as it almost always is at the screening level for outdoor-use pesticides because "may affect" is interpreted broadly), EPA has two options: it can enter into formal consultation or proceed to Step 2—an optional step known as informal consultation—in which it must determine whether the action is "likely to adversely affect" a listed species. If the answer is no and NMFS or FWS concurs, the consultation process ends. However, if the answer is yes, Step 3 (formal consultation) is triggered. In formal consultation, NMFS or FWS must determine whether the action is "likely to jeopardize the continued existence of the species." A jeopardy decision must be informed by science, but the final regulatory determination of whether a risk is sufficient to constitute jeopardy is partly a policy decision. As the action agency, EPA is responsible for Step 1. It is also responsible, with concurrence from the Services, for Step 2; the Services are responsible for Step 3. In 2004, the Services promulgated a rule that would essentially authorize EPA to conduct Step 2 on its own without concurrence from the Services. The court found that this was a violation of the ESA, and it invalidated that portion of the Services' rule [*Washington Toxics Coalition v U.S. Fish & Wildlife Serv.*, 475 F.Supp.2d 1158 (W.D. Wash. 2006)]. In recent years, EPA seems to be bypassing Step 2 and initiating formal consultation whenever it finds that a pesticide "may affect" a listed species. Although this approach is permissible, it might be more efficient in many cases to conduct a Step 2 analysis before deciding to enter formal consultation. Presumably, Step 2 would filter out some actions, and fewer biological opinions would be needed. An agreed-on common approach to ERAs would give the Services more confidence in EPA's Step 2 analyses.

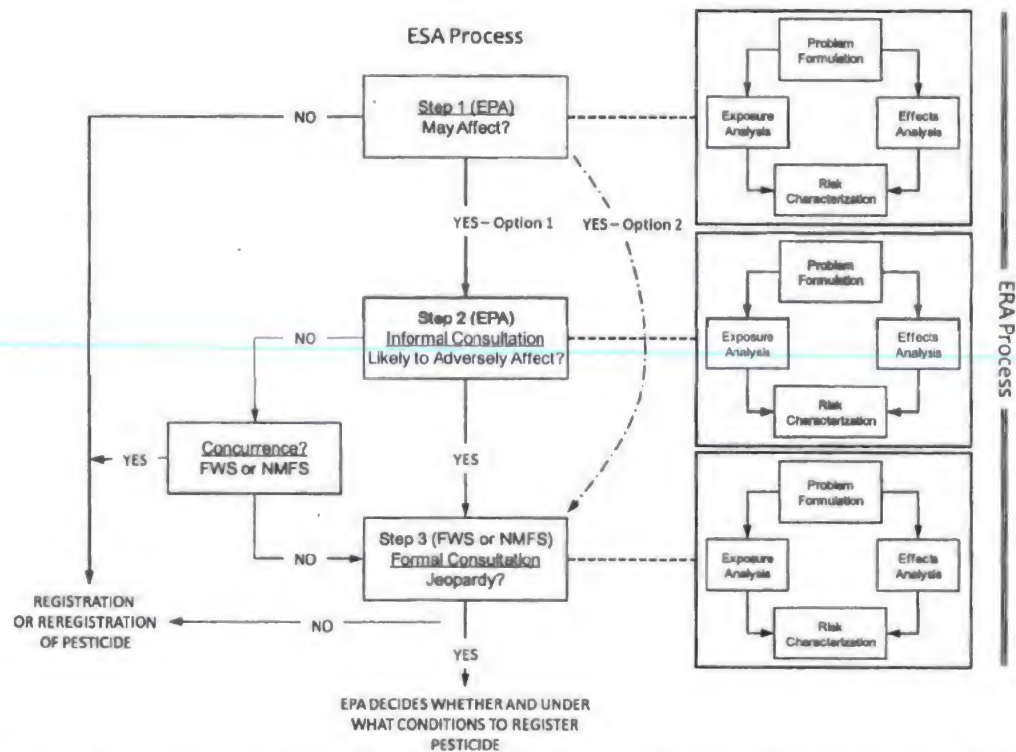


FIGURE 2-1 Relationship between the Endangered Species Act (ESA) Section 7 decision process and the ecological risk assessment (ERA) process for a chemical stressor. Each step answers the question that appears in the box.

As shown in Figure 2-1 and summarized in Table 2-1, the committee is suggesting that each step in an ESA consultation process for a chemical stressor be coordinated with an ERA process. Although the complexity of each ERA would depend on the step, each would involve the same four basic elements—problem formulation, exposure analysis, effects (or exposure-response) analysis, and risk characterization—that make up a risk assessment of a chemical stressor, such as a pesticide. The four basic elements and their relationships to one another trace their origin to the seminal *Risk Assessment in the Federal Government: Managing the Process* (NRC 1983; commonly referred to as the Red Book) and, more recently, to *Science and Decisions: Advancing Risk Assessment* (NRC 2009; commonly called the Silver Book). After 30 years of use and refinement, this risk-assessment paradigm has become scientifically credible, transparent, and consistent; can be reliably anticipated by all parties involved in decisions regarding pesticide use; and clearly articulates where scientific judgment is required and the bounds within which such judgment can be made. That process is used for human-health and ecological risk assessments and is used broadly throughout the federal government (for example, by the Food and Drug Administration). The committee notes that the *Services' Consultation Handbook* is silent regarding technical approaches to assessing risks to listed species posed by chemical stressors, such as pesticides. Consequently, the committee has concluded that the risk-assessment paradigm reflected in the ERA process is singularly appropriate for evaluating risks to ecological receptors, such as listed species, posed by chemical stressors, such as pesticides.

TABLE 2-1 Steps in the ESA Process as Related to Elements in the ERA Process for Pesticides^a

Step in ESA Process [Responsible Agency]	Element of the ERA Process		
	Exposure Analysis (Chapter 3)	Effect (Exposure-Response) Analysis (Chapter 4)	Risk Characterization (Chapter 5)
1 [EPA] Determine whether use of a pesticide "may affect" any listed species	Distribution of listed species in space and time	Distribution of the pesticide in space and time if used as labeled (toxicity is assumed)	Possibility that species and pesticide distributions would overlap in space and time
2 [EPA] Determine whether use of a pesticide is "likely to adversely affect" any listed species	Modeled exposure concentrations	Exposure-response function for an individual receptor's survival and reproduction	Probability of adverse effects on survival and reproduction of individual receptors
3 [SERVICES] Determine whether use of a pesticide is likely to cause "jeopardy"	Modeled or measured exposure concentrations	Exposure-response functions for survival and reproduction rates	Probability of adverse effects on population viability over space and time

^aSee section "Coordination among Agencies" for a discussion of problem formulation, the first element of the ERA process.

Although the ERA process should always include the four elements, the content of each is expected to change as the question shifts from whether a pesticide "may affect" a listed species (Step 1) to whether it is "likely to affect" a listed species (Step 2) to whether the continued existence of the listed species is likely to be jeopardized (Step 3). Consistency of the basic ERA process throughout the three steps (if all are needed) is the first essential point. The second is that each ERA becomes more focused and specific to the chemicals and species of concern as it moves from Step 1 to Step 3. The third point is that the Services should build in Step 3 on what EPA did in Steps 1 and 2; they should not start over with a separate and different analysis in Step 3.

Thus, the committee envisions the following process. In Step 1, EPA would consider whether *any* listed species might be harmed by the pesticide simply by asking whether areas proposed for pesticide application and known (or suspected) species ranges or habitats coexist. Not all listed species exist everywhere, nor are all pesticides used everywhere, so that simple formulation of the problem would help to narrow the scope of later assessments. In Step 2, EPA would address the question of whether the use of a pesticide in the specific context of its proposed patterns of use is "likely to adversely affect" one or more listed species or their critical habitats. EPA would approach that question from a chemocentric viewpoint and estimate potential environmental concentrations and possible toxic effects. Essentially, EPA would evaluate whether the pesticide would be used in a manner that would result in environmental concentrations that have the potential to affect a listed species, other organisms in its habitat, or its critical habitat adversely. The assessment would be relatively generic (that is, not site-specific), and the effects analysis would focus on individuals of the listed species. If the predicted concentrations could adversely affect individuals in a population of a listed species, EPA would consult with the appropriate Service, which would then be responsible for a jeopardy determination. In Step 3, NMFS or FWS ideally would focus more specifically on potentially affected listed species in an ecological context and address the question of whether locally applicable predicted or measured exposures result in effects on the listed species or on other species in their habitats in a manner that would change the ability of a population to persist or to recover or that would change the time to extinction.

The possible differences in risk assessments between Steps 2 and 3 in the ESA process can be seen by considering that the imaginary pesticide X—designated PX for this discussion—will be applied to wheat in Illinois in summer. In this hypothetical example, EPA decides that because PX is used in a region where there are listed sturgeon species, some PX could get into streams and possibly affect the fish. So, the agency progresses to Step 2. Here, problem formulation is used to narrow the assessment's scope by asking two questions: Are there any organisms for which we know that the pesticide is nontoxic (for example, exposures at greater than 5,000 ppm cause no effect)? Are there any environmental media (water, soil, and air) in which the pesticide will not reside? Following problem formulation, EPA runs the standard farm-pond model to

determine an initial estimate of the probable concentration of PX in the water, recognizing that the farm-pond model might not accurately represent conditions that apply to flowing streams and rivers where sturgeon actually live. That concentration is compared with the toxicity threshold that is based on full life-cycle tests in standard laboratory species, and EPA also considers that sturgeon are generally more sensitive to PX-like chemicals for the assessment end point than are standard test species. EPA concludes that pesticide concentrations in streams could exceed toxicity thresholds at the proposed application rates and notes further that PX-like chemicals can cause sublethal effects, including behavioral changes and darker color in adults. PX also kills aquatic invertebrates (the prey base of sturgeon) at concentrations lower than ones that affect sturgeon. On the basis of those results, EPA reaches a conclusion of "likely to adversely affect" and institutes formal consultation with the Services as required.

FWS builds on EPA's analysis in Step 3 and uses site-specific data on Illinois soils to calculate potential runoff to the slow-moving rivers and streams favored by sturgeon during summer. Because of the high clay content of the soils, PX binds to the root zone, and little is expected to move through soil into the streams. However, surface runoff—particularly during heavy rains, when a lot of soil is lost from fields—can result in water concentrations above effect concentrations. FWS reviews the information on behavioral effects and concludes that the studies are not reliable indicators of field effects. It also concludes that a darker color induced by PX exposure would increase the probability of survival of the fish because they would be more mud-colored and therefore better camouflaged. Because of concern about potential effects of PX on sturgeon in areas of the state that have a potential for substantial soil loss during summer rain events, FWS runs a spatially explicit population model to determine whether there could be a reduction in reproductive output that would affect the recovery of the population; it determines that changes in the growth rate of the population are unlikely. Furthermore, FWS concludes that the effects on aquatic invertebrates occur during times of the year when young sturgeon (the insectivorous life stage) are not present. Therefore, FWS reaches a conclusion of "no jeopardy."

In that hypothetical example, EPA and FWS use the same exposure models but different input parameters (generic farm-pond analyses vs site-specific soil runoff into shallow streams), assume different environmental transport pathways (surface runoff vs below ground), incorporate effects thresholds from the same studies, and review the same studies on sublethal effects. EPA uses reasonable worst-case assumptions of effects of PX on individual fish to reach a "likely to adversely affect" conclusion, whereas FWS uses site-specific data, incorporates spatial variability, and bases its decision on changes in population growth rates to reach a finding of "no jeopardy."

The committee concludes that using a common approach would eliminate many problems in assessing risks to listed species that are being encountered by EPA and the Services. As noted by Suter (2007, p. 37), the "advantages of using a single standard framework include familiarity and consistency, which

reduce confusion and allow comparison and quality assurance of assessments.” The ERA process that has evolved over the decades is best suited to evaluating the risk to listed species and their critical habitats posed by pesticides, and, as noted by Suter (2007, p. 37), the “EPA framework is a preferred default for ecological risk assessment in the United States.” Although the committee does not expect the basic risk-assessment framework to change, it recognizes that risk-assessment approaches and methods for determining, for example, what is hazardous, how much is hazardous, what end points constitute an adverse effect, and when, where, and how much exposure is occurring will continue to evolve.

COORDINATION AMONG AGENCIES

A letter from the Services to EPA in 2004 (Williams and Hogarth 2004) detailed previous efforts to reconcile the differences between EPA’s and the Services’ approaches to pesticide evaluation. That letter was followed, in the same year, by an alternative consultation agreement between EPA and the Services. Although all six tasks assigned to the committee were discussed in that letter and the later agreement, the extent to which the agreement was implemented remains unclear. The committee emphasizes that given the changing scope of the ERA process from Steps 1-3, EPA and the Services need to coordinate to ensure that their own technical needs are met.

First, before a risk assessment is even initiated, the agencies need to connect the decision that must be made with the risk assessment that will inform it. That stage, often referred to as planning and scoping (EPA 1998, 2004), involves a team of decision-makers, stakeholders, and risk assessors who identify the problem to be assessed, develop a common understanding of why the risk assessment is being conducted, and establish the management goals of the assessment. Decision-makers can identify information that they need to make decisions, and risk assessors can ensure that the science meets the needs of decision-makers and stakeholders. Together, all stakeholders should be able to evaluate whether the assessment is likely to address the identified problems with the desired confidence (EPA 2004).

Second, problem formulation, conducted as part of the ERA process (see Figure 2-1), could provide an effective means for EPA and the Services to coordinate and reach agreement on many of the key technical issues involved in assessing risk posed to listed species by pesticides. Problem formulation frames the risk-management objectives sufficiently for the risk assessor to identify all potential inputs into the risk-assessment model. Guided by the needs of the decision-makers and using the best data available, the risk assessor develops a conceptual model of stressor sources, exposure pathways, and receptors; poses risk questions or hypotheses; and identifies the methods and analyses that will be used to address the questions and hypotheses. If problem formulation is successful, a comprehensive, scientifically credible conceptual model will be developed, there will be agreement on the risk-assessment approach, and the output of

the assessment will have sufficient specificity for decision-making. The analysis phase of the risk assessment should not begin until the decision-makers are satisfied that the risk assessor understands the questions that need to be addressed and understands how much confidence in the final risk estimate is needed. Problem formulation is also an excellent time to discuss how the risk estimate will be communicated at the conclusion of the assessment.

The committee views coordination among EPA and the Services as a collegial exchange of technical and scientific information for the purpose of producing a more complete and representative assessment of risk, including the types and depths of analyses to be conducted at each step in the process. Such coordination would allow EPA's expertise in pesticides to be effectively combined with the Services' expertise in life histories of listed species and in abiotic and biotic stressors of the species. Coordination discussions would include many of the issues discussed by the committee in the present report, such as datasets to use to delineate species' habitats, the need for additional fate data, and new approaches for exposure and effects analysis. The agencies can use Steps 1-3 as a framework for such discussions but need not be constrained by them. It might be that technical working groups would form around various aspects of the assessment approach—such as fate and transport modeling, estimating species distributions and habitats, data-sharing, and uncertainty analysis—to discuss technical details and that others would discuss policy-based issues, such as which evolutionarily significant units to include in the analysis. The committee recommends that such collaboration meetings be formal, structured workshops that have stated goals and objectives, be led by professional facilitators, and have formal agendas agreed to by all parties. That approach would enhance productivity and allow expectations to be met. The periodicity of such discussions would necessarily be at the discretion of the agencies, but the committee recommends a frequency of at least once every 2 years to capture updates in risk-assessment and population-biology methods, newly listed species, new pesticide classes, and changing agricultural practices.

The committee concludes further that coordination during problem formulation regarding the ESA and ERA processes would be enhanced if a common outline, such as the one shown in Box 2-1, were adopted. The details of the outline would be adapted according to the step being conducted. However, the outline should incorporate specific elements of concern and interest to EPA and the Services. For example, examination of earlier EPA assessments has revealed a need for EPA to include and consider all available information about the life history of a listed species early in the process, ideally during planning and scoping (Item 1.1.4 in Box 2-1). Although assessment end points might ultimately involve only common surrogate or test species, the inclusion of natural life-history information on the listed species and critical habitat would at least enable a qualitative assessment of the similarities and differences between the listed species and the identified surrogates.

BOX 2-1 Generic Outline for Reporting Ecological Risk-Assessment Results for Listed Species or Their Critical Habitats

1. PROBLEM FORMULATION
 - 1.1. Background
 - 1.1.1. Defining the Regulatory Action
 - 1.1.2. Nature of the Pesticide
 - 1.1.3. Pesticide-Use Characterization
 - 1.1.4. Natural History of Listed Species
 - 1.1.5. Designated Critical Habitats
 - 1.2. Action Area (based on use and natural history)
 - 1.3. Assessment End Points
 - 1.3.1. Individuals
 - 1.3.2. Populations
 - 1.3.3. Critical Habitats
 - 1.4. Conceptual Model
 - 1.4.1. Risk Questions or Hypotheses
 - 1.4.2. Graphical Representation
 - 1.5. Analysis Plan
 - 1.5.1. Measures (exposure, effect, and characteristics)
 - 1.5.2. Approach to Risk Estimation
2. EXPOSURE ANALYSIS
 - 2.1. Label Application Rates and Intervals
 - 2.2. Habitats of Listed Species
 - 2.3. Exposure (Transport and Fate) Modeling
 - 2.3.1. Aquatic Organisms
 - 2.3.2. Terrestrial Organisms
 - 2.4. Exposure to Mixtures
 - 2.5. Monitoring Data
 - 2.6. Exposure Estimate (with uncertainty)
3. EFFECTS ANALYSIS
 - 3.1. Incident Database Review
 - 3.2. Individuals
 - 3.2.1. Direct Effects (acute, sublethal, and chronic)
 - 3.2.2. Indirect Effects
 - 3.3. Effects on Critical Habitats
 - 3.4. Mixture Effects
 - 3.5. Exposure-Response Estimate (with uncertainty)
4. RISK CHARACTERIZATION
 - 4.1. Risk Estimate
 - 4.1.1. Individuals
 - 4.1.2. Populations
 - 4.1.3. Critical Habitat
 - 4.2. Field and Laboratory Comparisons
 - 4.3. Risk Description (integration and synthesis)

UNCERTAINTY

The committee was asked to consider the interpretation of uncertainty and specifically the selection and use of uncertainty factors to account for lack of data. However, before the committee can answer the question about uncertainty factors, it must consider how uncertainty has been treated in past assessments. The committee addresses the question about uncertainty factors in Chapters 4 and 5.

In the context of this report, risk is defined as the probability of adverse effects on listed species or their critical habitats due to anticipated pesticide use that is consistent with label requirements. Ultimately, the adverse effect is jeopardy to the continued existence of a listed species defined in terms of demography, habitat, or other resources. The risk is estimated on the basis of predicted future pesticide exposure concentrations and the type and magnitude of effects (as determined by exposure-response functions) that the pesticide could have on the species. The risk estimate reflects uncertainty due to natural variability, lack of knowledge, and measurement and model errors in the host of underlying assumptions and variables used to predict exposure and effects. Natural variability or variation is true heterogeneity that might be better defined (but never eliminated) through increased sampling. Lack of knowledge (ignorance) is due to an absence of data or incomplete knowledge of important variables or their relationships; it can be reduced through additional data collection or further research. As indicated in Box 2-1, uncertainty will need to be characterized in the exposure estimation (Item 2.6) and the effect-response estimation (Item 3.5) analyses, then propagated, and finally integrated (Item 4.3) to provide the risk as a probability with an estimate of uncertainty.

The committee has concluded that achieving such integration will require that the ERA process in Steps 2 and 3 adopt a probabilistic approach that allows uncertainty in exposure and effect to be explicitly recognized and then combined to yield a risk as a probability with associated uncertainty (see Chapter 5). The present practice of relegating the consideration of uncertainty to a separate, often qualitative, narrative at the end of an assessment is of marginal value because doing so has little notable effect on risk estimation itself or on a decision-maker's ability to understand the confidence that should be placed in a risk estimate. Although the committee is aware of the administrative and other nonscientific hurdles that will need to be overcome to implement such an approach, it nonetheless has concluded that moving the uncertainty analysis from a narrative addendum to an integral part of the assessment is both possible and necessary to provide realistic, objective estimates of risk. Because a core dataset is required for all pesticide registration decisions, there should be sufficient information to conduct a quantitative assessment, which can include a quantification of the associated uncertainty.

The committee recognizes that the quantitative propagation of uncertainty through ecological risk assessments is not a new concept, particularly in the context of pesticide assessments. The topic was addressed by EPA's Scientific Ad-

visory Panel for FIFRA in 1996 (Bailey et al. 1997) and was explicitly addressed in a workshop held in 2009 (Warren-Hicks and Hart 2010). EPA has since developed and begun to implement the Terrestrial Investigation Model (TIM; Odenkirchen 2003); TIM version 2.0 includes Monte Carlo simulations for calculating pesticide concentrations in a simulated farm pond and estimating activity patterns of potentially exposed wildlife. The committee recognizes that the use of frequentist statistics and Monte Carlo simulations, although widespread, is only one approach to quantifying and propagating uncertainty through an ERA. Bayesian approaches to environmental assessments, some of which also use Monte Carlo simulations, have become more widely understood and more feasible over the last few decades as computational power and capability have improved (Ellison 1996; McCarthy 2007; Link and Barker 2010). For example, Borsuk and Lee (2009) describe the application of Bayesian approaches to increase environmental realism in population modeling, and Reckhow (1999) applies similar approaches to water-quality predictions. Their applicability to analyses of data on chemicals and to other environmental risk assessments (Clark 2005), including those for endangered species, has been recognized in the federal government (FDA 2010; Conn and Silber 2013), although they have not yet been widely adopted for chemical risk assessment. Bayesian methods reliably estimate modeled variables, and Bayesian models can readily propagate uncertainties in data (such as measurement errors) and uncertainties in model structure (such as selection of covariates and relationships among them). The models can incorporate data from multiple sources, expert knowledge, and empirical evidence about relationships among variables and about the shape of the data distributions; however, these are not required to use or run the models. Bayesian approaches are most useful during Step 3 of ESA pesticide analyses when an in-depth analysis is needed, such as when alternative pesticide-use scenarios or proposed mitigation actions might have large spatial or economic consequences.

EPA has noted that “the explicit treatment of uncertainty during problem formulation is particularly important because it will have repercussions throughout the remainder of the assessment” (EPA 1998, p. 26). For ESA Section 7 consultations on pesticide risk to listed species, it is likely that the amount of data available for producing a risk estimate will vary by species and by chemical. The risk assessor will therefore need to ascertain during problem formulation how much confidence in the risk estimate the decision-maker requires to support a decision, given the decision context. Does the decision-maker need a risk estimate with low uncertainty or is, for example, $\pm 25\%$ acceptable? Decisions regarding uncertainty need to be balanced with a discussion about availability of time and resources and need to consider the extent to which uncertainties are unavoidable given likely data gaps. A quantitative analysis of expected value of information could be conducted to answer the question of whether the reduction in uncertainty warrants obtaining more information (Yokota and Thompson 2004; Runge et al. 2011; Moore and Runge 2012). However, the committee recognizes that time limitations might preclude such an analysis (Yo-

kota and Thompson 2004). The committee acknowledges the utility of a qualitative assessment and discussion between risk assessors and decision-makers at both Step 2 and Step 3 of the ESA risk-assessment process. A decision-maker will then be adequately informed about the estimated probability of an adverse effect and can make a decision about whether the proposed action is “likely to adversely affect” or can be “reasonably expected” to result in jeopardy. Decisions about the acceptable level of risk and how to manage the risk are policy decisions that are not part of the scientific analysis.

The committee recognizes that decision-makers will need to understand how to interpret and use the information on uncertainty in their decision-making. There is a great body of literature on risk management and decision-making under uncertainty that can help to guide and guard against misuses of uncertainty in decision-making (see, for example, Cropper et al. 1992, Morgan and Henrion 1992, EPA 2010, and IOM 2013).

BEST DATA AVAILABLE

As discussed in Chapter 1, the Services have a mandate to use the “best scientific and commercial data available” in their assessments. There is little guidance on what constitutes “best data available,” and the agencies do not appear to have formal protocols that define “best data available.” However, the following sections describe the agencies’ approaches to data collection and evaluation, and the committee provides some guidance on important data characteristics.

Scope of Data Collection and Selection

EPA (1998) indicated that a search for all available data is conducted at the start of each risk assessment and iteratively throughout the assessment to support and guide each step of the process. EPA’s primary repository for peer-reviewed toxicity studies that are publicly available is ECOTOXicology (ECOTOX; EPA 2012a). The Services and EPA agreed to use ECOTOX as the common source for data on ecotoxic effects of pesticides (EPA 2011).

Data used by EPA in pesticide risk assessments are typically derived from detailed reports of standardized studies required for pesticide registration under FIFRA; studies in peer-reviewed journals or other publications, such as reference books; and government reports and surveys. Repository databases are used if they meet data-quality standards. The Services also include anecdotal or oral information and other unpublished materials from such sources as state natural-resources agencies and natural-heritage programs, tribal governments, other federal agencies, consulting firms, contractors, and persons associated with professional organizations and institutions of higher education (59 Fed. Reg. 34275 [1994]). Accordingly, the scope of data collection by the Services appears

broad, although some of the information collected can be brief and be insufficient for independent evaluation.

Evaluation of Data Relevance and Quality

Information on pesticides and the ecology of listed species that is used in risk assessments should be both relevant and of high quality. Relevance refers to information that is consistent with its intended use. Accordingly, the information should be from studies of the species and chemicals being assessed, or there should be a strong theoretical basis for extrapolation to the species and chemicals being assessed. The information should be spatially applicable to the locations being considered and be sufficiently recent to be pertinent. For example, information on the environmental transport and fate of the specific pesticide active ingredient under review or of the class to which the pesticide belongs would be relevant to the assessment. Similarly, information on the ecology of the listed species is highly relevant and useful particularly if it has been obtained recently from the area of pesticide use. Conversely, a study that used a population census of the listed species conducted 20 years ago would not be relevant. Information that is not relevant clearly should not be used to assess risk, and the question of relevance is the first question that needs to be addressed in considering whether information should be used for a risk assessment.

The quality of the relevant information should be reviewed before it is used in a risk assessment. A critical question to answer is whether the data conform to best scientific practice. Best practice includes providing sufficient information that characterizes the data (such as who collected them, when and where they were collected, what variables were measured, and how and in what units measurements were taken), clear methods that would allow a third party to replicate the data-collection process or the analyses conducted with the data, and estimates of data accuracy or uncertainty. If sufficient information is not available, data quality is unknown, and the data should be given less prominence in the risk assessment. Accordingly, data of lower quality should not be used to nullify data of higher quality. Ideally, data are objective and unbiased, although failure to meet those requirements might not be a cause for rejection if biases are sufficiently described and clearly identified in the assessment.

EPA has a formal set of data relevance and quality criteria that are applied in selecting information for use in regulatory assessment. The EPA Science Policy Council published a set of five assessment factors for evaluating scientific and technical information on the basis of EPA practices, input from the public, and results from a workshop hosted by the National Academy of Sciences (EPA 2003). The assessment factors are intended to improve data generation, use, and dissemination in EPA and by the data-generating public. The assessment factors are *applicability and utility* (relevance of the information to its intended use and applicability to the current scenarios of concern), *soundness* (scientific validity of experimental study, survey, modeling, and data collection and adequate sup-

port for conclusions), *clarity and completeness* (documentation that includes underlying assumptions, study protocol and design, data accessibility, and data analysis), *uncertainty and variability* (quantitative and qualitative characterization, effect on conclusions, and the identification of parameter values that, if changed, would substantially affect the outcome of the model), and *evaluation and review* (independent verification, validation, and peer review and consistency with results of similar studies). The EPA Office of Pesticide Programs has additional guidelines for acceptance of scientific literature, as described in the documentation supporting the ECOTOX database (EPA 2012b).

FWS and NMFS do not have agency-specific guidelines on data relevance and quality. However, all federal agencies are expected to comply with the Office of Management and Budget (OMB) guidelines on objectivity, utility, and integrity of disseminated information. OMB (67 Fed. Reg. 8452 [2002]) describes those attributes as follows:

“Objectivity” focuses on the extent to which information is presented in an accurate, clear, complete and unbiased manner; and, as a matter of substance, the extent to which the information is accurate, reliable and unbiased. “Utility” refers to the usefulness of the information to the intended users. “Integrity” refers to security, such as the protection of information from unauthorized access or revision, to ensure the information is not compromised through corruption or falsification.

The Services and EPA (EPA 2002; FWS 2007) have separately published information quality guidelines (IQGs) that follow closely the government-wide OMB guidelines. Similar basic principles for achieving a scientifically credible assessment are prescribed in the IQGs from the agencies; the agencies are committed to ensuring the quality of evaluations and the transparency of information from external sources used in their disseminated assessments and actions (EPA 2003; NMFS 2005). They also recognize that a high level of transparency and scrutiny is needed for influential information that is expected to have a substantial effect on policies and decisions (EPA 2002; NMFS 2004; FWS 2007).

In the biological opinions provided, the committee was able to discern at least one approach that the Services use to evaluate relevance and quality of data. In the ESA consultation for assessing the effects of 12 organophosphates on salmonids (NMFS 2010), NMFS described and used a qualitative set of evaluation criteria. Three criteria were used to judge the relevance of the publicly available toxicity data: whether the studies were conducted on salmonids, whether they measured end points of concern, and whether they evaluated effects of exposure to the specific chemicals or structurally related chemicals. The more criteria were met, the more relevant the studies were deemed. A fourth criterion was related to data quality and had to do with whether relevant studies had substantial flaws in experimental design.

Important Data Characteristics

Data relevance and data quality clearly are primary factors in determining whether data constitute "best available data." Several data characteristics noted in the committee's charge and described below are related to relevance and quality and can help to determine whether data are useful for assessing the risk to listed species posed by pesticides.

Validity. Data that are used in risk assessment should be accompanied by sufficient information for repeatability, independent scientific review, and additional data analysis when needed (NRC 1995). For example, an additional analysis, such as a dose-response analysis, might be necessary to ensure accurate interpretation of the data. Data sources that lack sufficient details for an adequate scientific evaluation—such as poster presentations, abstracts, anecdotal or personal communications, and data files that contain no information on fundamental data attributes—might provide background knowledge or support an overall weight-of-evidence evaluation but should not be the sole basis for drawing assessment conclusions. Thus, although secondary information can be useful for identifying an original report, it should not be used directly in risk assessment. The original study is necessary for an independent review of accuracy, quality, and relevance. An example from the draft biological opinion on the effects of 2,4-dichlorophenoxyacetic acid (2,4-D) on salmonids illustrates the problems with using secondary sources. That biological opinion cited Brock et al. (2000), which attributed a value for an aquatic-community effect to a report by Boyle (1980), but the effect cited was not found in the primary source.

Availability. Many data used in pesticide risk assessment are taken from unpublished studies that are conducted to support pesticide registrations. Those studies are conducted according to well-defined protocols and prescribed good laboratory practices. The detailed reporting allows EPA scientists to evaluate study quality independently and to conduct data analysis beyond what is possible with studies published in the open literature.¹ EPA's evaluation is documented in a data evaluation record (DER), which contains information on study methods, results, and discussions. Additional data analysis or modeling is also documented. Recent DERs, in contrast with older ones, can serve as stand-alone reports based on full study reports submitted for pesticide registration. Public availability of DERs is important because the submitted studies are typically protected confidential business information (CBI) and not publicly available or readily accessible. However, other government agencies, such as NMFS and FWS, can review CBI once necessary information controls are in place and therefore provide data-quality assurance for EPA's reported information on in-

¹As noted in Chapter 1, the Services do not have the authority under the ESA to require the generation of data but instead must rely on the best data that are available. Furthermore, the ESA makes it clear that the Services are not to delay action because of a lack of data.

dustry studies. In addition, EPA has increased public access to DERs in recent years by making more information available to the general public. The committee encourages EPA to continue to share the studies with the Services, to provide sufficient details in DERs to ensure a reasonable understanding of the studies, and to make DERs readily available to the public.

Consistency. Data consistency is an important consideration in drawing scientific inferences. Apparently conflicting results from different studies should be examined with care. Different results from studies that use different species, life stages, exposure regimens, observation methods, experimental conditions, or statistics do not necessarily constitute conflicting evidence, and all might be useful in drawing conclusions. However, statistical outliers should be given particular scrutiny to verify the quality of an underlying study, particularly if they differ from all other data by orders of magnitude.

Clarity. The strengths and weaknesses of data and the reason that they were or were not used in a risk assessment should be clearly documented. Expert opinion or judgment is also used in risk assessment and is valuable especially when uncertainty is high because of data gaps. However, it is important that the assumptions or judgments be clearly described. As stated in NRC (1995), a clear presentation of expert knowledge should include the line of reasoning used and should separate facts from speculation. Similarly, adequate rationale should be given throughout the assessment for the assumptions that are made in the absence of data.

Utility. Utility clearly is related to relevance. One specific issue that has arisen regarding utility concerns the usefulness of foreign-language articles. Studies might be excluded by EPA because of a language barrier and lack of funding to obtain an English translation. For example, foreign-language reports, especially ones that are not readily available in the open literature, might be included in ECOTOX but not used in a risk assessment. If foreign-language reports are used in a risk assessment, translated versions will be needed so that the data in the reports can be subjected to the same data quality and relevance evaluation as data from studies published in English.

Peer Review. Regardless of the data criteria, it is not unusual for well-qualified risk assessors to disagree on the quality of data or on their relevance to a specific assessment. Because OMB attaches stricter requirements to discretionary peer review of highly influential scientific assessments (Bolten 2004), the committee emphasizes the value of external peer review to enhance the quality, transparency, and credibility of a risk assessment.

CONCLUSIONS AND RECOMMENDATIONS

A Common Approach and Coordination among the Agencies

- Lack of a common approach has created scientific obstacles to reaching agreement between EPA and the Services during consultation.

- The risk-assessment paradigm, as reflected in the ERA process, is a scientifically credible basis of a single, unified approach for evaluating risks to listed species posed by pesticide exposure under FIFRA and the ESA.
- The committee's recommendation is that the ERA process include the same four elements (problem formulation, exposure analysis, effects analysis, and risk characterization) at each step but that the content of each changes as the question shifts from whether the pesticide "may affect" a listed species (Step 1) to whether it is "likely to adversely affect" a listed species (Step 2) to whether the continued existence of the listed species is jeopardized (Step 3).
- The ERA process would be enhanced if it were accompanied by use of a common outline that incorporates specific elements of concern to EPA and the Services.
- Given the changing scope of the ERA process from Step 1 to Step 3, EPA and the Services should coordinate to ensure that their own technical needs are met.
- Problem formulation, conducted as part of the ERA process, could be an effective way for the agencies to coordinate and reach agreement on many of the key technical issues involved in assessing risks posed by pesticide exposure.

Uncertainty

- Risk assessments and jeopardy decisions require recognizing and analyzing uncertainty and quantitatively propagating it through any assessment so that it is clearly reflected in the eventual risk estimate.
- The agencies should adopt a probabilistic approach that allows uncertainty in exposure and effect to be explicitly recognized and then combined in forming a risk estimate.
- Although administrative and other nonscientific hurdles will need to be overcome to implement such an approach, changing uncertainty analysis from a narrative addendum to an integral part of the assessment is possible and necessary to provide realistic, objective estimates of risk.
- Decisions about acceptable levels of risk and how to manage risk are policy decisions that are not part of the scientific analysis.

Best Data Available

- The agencies do not appear to have formal protocols for defining "best data available" and appear to approach data collection and selection from different perspectives.
- To ensure that the best data available are captured, a broad data search is needed at the beginning of the process. Dates of searches and search strategies should be clearly documented to ensure transparency of the process. If a repository database is searched, its contents and scope should be described, including

criteria for data inclusion and exclusion, periodicity of updates, and quality control for data entry.

- Given that stakeholders are aware of and can provide valuable and relevant data, the committee encourages provision for their involvement at the early stage and throughout the ERA process. Stakeholder data are expected to meet the same data relevance and quality standards as all other data.
- To ensure that the best data available are used, information should first be screened for relevance and then subjected to quality review.
- The agencies should, at a minimum, subject all information to a review based on OMB criteria of "objectivity, utility and integrity." Information sources that fail any of the criteria can be used at the discretion of the risk assessor, provided that their limitations are clearly described.
- Comparisons of all information sources with the relevance and quality attributes should be documented in the risk assessment and described in the overall characterization of uncertainties.

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3

Exposure

The committee was asked to consider various issues associated with models, geospatial data, mixtures, and uncertainty. Although the language of the task statement was focused on effects analysis, determining which effects might be relevant requires estimating exposure. In this chapter, the committee first discusses fate and transport models used in exposure analyses by the agencies and then provides suggestions for a stepwise approach to estimating environmental concentrations of pesticides in the context of complying with the Endangered Species Act (ESA). Next, the committee addresses what constitutes authoritative geospatial data—critical information used to conduct exposure modeling and define species' habitats—and provides some examples. Finally, the committee discusses some important uncertainties associated with exposure analysis and the need to propagate uncertainty through the analysis.

EXPOSURE-MODELING PRACTICES

If pesticides are to be used without jeopardizing the survival of listed species and their habitats, the estimated environmental concentrations (EECs) to which the organisms and their habitats will be exposed need to be determined. Chemical fate and transport models are the chief tools used to accomplish that task. Broadly, such a model requires a user to choose a series of environmental control volumes—that is, environmental compartments containing multiple media, such as air, water, and soil—that are assumed to have a single, homogeneous pesticide concentration at each time step of the model. The transport and transformation processes that might affect a pesticide's presence in each control volume are combined and assembled into a mass-balance model that allows estimation of the EECs. Typically, the fate processes, such as sorption and biodegradation, are mathematically expressed in such a way that they can be adjusted by using chemical-specific and environment-specific information. However, knowledge or information can be insufficient, so the model parameter values for some chemical or physical processes are often oversimplified. For example, the distribution of a pesticide between the solids and water in a single compartment might be quantified by using a linear adsorption isotherm, although the data might suggest that the pesticide sorption mechanism exhibits nonlinear behavior.

Because the pathways by which pesticides move from their points of application to habitats of listed species might involve a complex sequence of transfers and diverse degradation processes, it is common to use a linked series of models to estimate exposure. Fate and transport modeling practices used by the US Environmental Protection Agency (EPA), Fish and Wildlife Service (FWS), and National Marine Fisheries Service (NMFS) are discussed below. The committee also elaborates on its suggestions for analyses that comply with Steps 1-3 in the ESA process when estimating exposure (see Table 2-1).

Approaches and Models Used by the Agencies

In Step 1 of the ESA process, EPA uses a program called DANGER to determine which listed species or their habitats coincide geographically and temporally with areas of pesticide use (EPA 2012a).¹ DANGER is an electronic database of county-level information on occurrence of listed species and acreage of agricultural crops. If there is geographic and temporal overlap, EPA assumes a “may affect” for pesticide use and addresses the listed species during its pesticide risk assessment (Step 2), in which pesticide concentrations are estimated in the environmental media to which the species might be exposed, as discussed below.

In Step 2 of the ESA process, EPA first uses a generic screening model to determine whether the pesticide is likely to move off the crop and into a body of water in concentrations high enough to trigger a concern for any aquatic species. For that initial screen, EPA uses GENEEC2 (Generic Estimated Environmental Concentration) (EPA 2001), a model that estimates pesticide concentrations in a standard small farm pond (a 2-m deep pond that has a surface area of 1 hectare in a watershed area of 10 hectares), uses generic inputs, and simulates a single event. Few fate processes are considered in the model. EPA typically assumes the maximum pesticide application rate as allowed by the label, and the model estimates pesticide concentration in the pond on the basis of spray drift and runoff from a 6-in. rain event that lasts 24 h.

As a screening model, GENEEC is sometimes characterized as providing worst-case estimates of exposure. The term *worst-case*, however, is misleading and should be avoided. The documentation for the model does not use the term *worst-case* but states that GENEEC “may provide a good predictor of upper level pesticide concentrations in small but ecologically important upland streams” (EPA 2001). That conclusion is attributed to Effland et al. (1999), but they discuss general monitoring data in streams rather than specific field studies that might be used to evaluate the accuracy of GENEEC with respect to specified applications.

¹The committee understands that EPA now commonly refers to the DANGER database as LOCATES (A. Pease, EPA, personal commun., May 13, 2013).

If the initial screening assessment triggers a concern for any aquatic species, EPA uses more sophisticated models, such as the Plant Root Zone Model (PRZM3; Suarez 2005) and the Exposure Analysis Modeling System (EXAMS; Burns 2004), to estimate pesticide concentrations in surface waters (EPA 2012b,c). Again, the standard farm field (10 hectares) and pond (1 hectare) scenario is typically modeled, but the models incorporate more fate processes and simulate effects of daily weather variability over multiple years. For example, the initial spatial fallout of a pesticide sprayed via aircraft into air over a field is estimated with a model, such as AgDRIFT® (Teske et al. 2002; SDTF 2010). The AgDRIFT-derived estimates then serve as inputs into PRZM3, which assesses pesticide fate in the soil environment, including evaporation to the atmosphere, infiltration into the subsurface, and off-site transport via overland runoff. Finally, to the extent that the combination of AgDRIFT and PRZM3 (which includes the Vadose Zone Flow and Transport model subroutine) yields estimates of pesticide delivery to nearby surface waters, EXAMS is used to estimate the temporally changing chemical concentrations in those waters and their underlying sediments. The resulting estimated concentrations in soil, water, and sediment yield estimates of the pesticide exposure of receptors of interest, including listed species.

For terrestrial species, EPA models pesticide exposure with the Terrestrial Residue Exposure (T-REX) model, the TerrPLant model, the Screening Imbibition Program (SIP) model, and the Screening Tool for Inhalation Risk (STIR) model (EPA 2012d). Exposure of terrestrial species is assumed to be through the diet, which is simulated by the exposure routine in T-REX. The model calculates pesticide residue concentrations on various food items (for example, short grass and broad-leaved plants) on the basis of work by Hoerger and Kenaga (1972) as modified by Fletcher et al. (1994) at a daily interval for 1 year. Other parts of the T-REX model translate exposure concentrations into daily doses for hypothetical small, medium, and large birds and mammals on the basis of food intake-rate equations from EPA's *Wildlife Exposure Factors Handbook* (EPA 1993). More recently, EPA has begun to estimate wildlife exposure through drinking water with the SIP model and inhalation with the STIR model. Those models are intended for use during problem formulation to determine whether the alternative exposure routes should be considered in the aggregate with food ingestion. SIP assumes that water concentrations are at the limit of solubility, and drinking-water ingestion rates are from Nagy and Peterson (1988). STIR calculates vapor-phase exposure from chemical-specific properties, such as molecular weight and vapor pressure, and includes estimates of spray-droplet exposure. Maximum inhalation rates are from EPA (1993), and the model assumes that a small-bodied bird or mammal is exposed to saturated air. For terrestrial plants, exposure for screening-level assessments of single pesticide applications is estimated by TerrPLant by assuming runoff delivery from a treated dry acre of land to a neighboring untreated acre, runoff from 10 treated acres to a 1-acre neighboring wetland, or specified percentages of spray drift after ground and aerial applications.

In Step 3, the Services also calculate environmental exposures with the same models that EPA uses in Step 2. For example, GENEEC2 was used in some of the biological opinions (BiOps) reviewed by the committee (NMFS 2008, pp. 235ff; 2009, pp. 284ff; 2010, pp. 294ff) as was AgDRIFT (NMFS 2008, p. 228). The committee did not examine any BiOps on terrestrial organisms, so it cannot comment on the terrestrial-exposure models used by the Services. However, the model input parameters used by NMFS to estimate aquatic exposure concentrations differ from those used by EPA, and the model is modified to estimate input into waters other than the standard farm pond. Those differences account for regional and habitat differences that are specific to the listed species and are discussed further in the next section.

A Stepwise Approach to Fate and Transport Modeling

Mass-balance models for chemical exposure analyses have several strengths. First, principles of mass-balance modeling and computer-simulation programs are well established. Second, many exposure models—such as AgDRIFT, PRZM, and EXAMS—are well documented. Third, the models can be made case-specific by time-varying data, such as meteorological conditions. Fourth, the output of one model can be used as input into the next one; for example, EXPRESS is a linked EXAMS-PRZM Exposure Simulation Shell (Burns 2006).

However, the model limitations need to be recognized, and models need to be used in the appropriate contexts. For example, GENEEC2 was developed by EPA simply as an easy-to-use screening tool to provide a consistent approach in the conduct of screening-level assessments, such as in Step 1 (or early in Step 2) of the ESA process (see Table 2-1). Although the Services have used GENEEC2 in BiOps, the committee concludes that a screening-level model has no place in Step 3 of the ESA process, in which the Services need to conduct a direct assessment of risk to a listed species. The GENEEC2 model has no provision for site-specific or region-specific inputs, such as soil characteristics, slopes, and meteorological data. Furthermore, with the development of simple-to-use implementations of PRZM/EXAMS for the farm pond and index reservoir (PRZM/EXAMS Express, Burns 2006), there seems to be little need for or practical value of GENEEC2. For Steps 2 and 3, EPA and the Services should be using region-specific or site-specific applications of PRZM/EXAMS or possibly more sophisticated watershed models.

As noted in Chapter 2 (see Table 2-1), the committee suggests a common approach that involves more refined and sophisticated modeling and analysis as one progresses from Step 1 to Step 3 in the ESA process. Given the current practices in exposure analysis and the need to estimate pesticide exposures and the associated spatial-temporal variations experienced by listed species and their habitats, the committee envisions the following stepwise approach to exposure modeling.

- *Step 1 (EPA)*. Initial exposure modeling would answer the question, Do the areas where the pesticide will be used overlap spatially with the habitats of any listed species? The Services, which have extensive knowledge of the natural history of listed species, could help EPA to identify overlaps of areas where a pesticide might be used and the habitats of listed species. EPA's DANGER program would be useful in this step.

- *Step 2 (EPA)*. If area overlaps are identified in Step 1, EPA would confer with the Services to identify relevant environmental compartments (for example, pond vs stream), associated characteristics (for example, sandy vs silty soils), and critical times or seasons in which environmental exposure concentrations need to be estimated. With that knowledge, suitable model parameter values could be chosen and used. The goal of EPA's initial exposure modeling would be to identify the most important environmental compartments for exposure modeling (water, soil, air, or biota). Models—such as GENEEC2, SIP, and SPIR—would be useful in this step. If the models indicate that substantial amounts of pesticides move off the application site and into the surrounding ecosystems, more sophisticated fate and transport processes could be incorporated. At that point, the pesticide-fate model could be simplified to remove processes that are unimportant in the specific regions of the listed species and set up to estimate time-varying and space-varying pesticide concentrations in typical habitats (for example, 10-cm-deep shallow regions along streams vs 2-m-deep farm ponds) with associated uncertainties. The committee emphasizes that inputs should include statistical distributions of each parameter to enable probabilistic modeling of exposure scenarios. During Step 2, EPA could direct the terrestrial exposure modeling at specific size classes of taxonomic groups that represent the listed species of concern. On the basis of the modeling results, EPA could then make a decision about the need for formal consultation with the Services.

- *Step 3 (Services)*. During a formal consultation, the Services would further refine the exposure models to develop quantitative estimates of pesticide concentrations and their associated distributions for the particular listed species and their habitats. To that end, the models would use site-specific input values—for example, actual pesticide application rates, locally relevant geospatial data to characterize such quantities as wind speed and organic contents of soils, and time-sensitive life stages of listed species. The exposure analysis would be completed with propagated errors on exposure estimates.

Some issues associated with the exposure models or modeling practices need to be emphasized. First, pesticide-fate models are not always well tested with field data for specific pesticide applications at sites whose properties are knowable. Bird et al. (2002) tested AgDRIFT, and Loague and Green (1991) tested PRZM. However, a comprehensive treatment of the use of EXAMS with pesticides is largely lacking. Burns (2001) did list six studies involving field observations of diverse compounds that could be compared with EXAM model-

ing expectations, but none of the data involved pesticides applied in agricultural settings except the use of sulfonyl herbicides in rice fields. To evaluate and improve the accuracy of the exposure estimates, one could pursue a measurement campaign specifically coordinated with several pesticide field applications in a few case-specific examples during Step 3 exposure modeling. The exposure estimates should be compared with pesticide measurements in various environmental media, and modeling should be revised if measurements deviate substantially from selected statistical bounds, such as two standard deviations, of modeled estimates of environmental concentrations.

The committee notes that in evaluating models, general monitoring data and field studies need to be distinguished. General monitoring studies (see, for example, Gilliom et al. 2007) provide information on pesticide concentration in surface water or ground water on the basis of monitoring of specific locations at specific times. The monitoring reports, however, are not associated with specific applications of pesticides under well-described conditions, such as application rate, field characteristics, water characteristics, and meteorological conditions. General monitoring data cannot be used to estimate pesticide concentrations after a pesticide application or to evaluate the performance of fate and transport models.

Second, the model predictions can be only as accurate as the parameter estimates. If the relevant parameter values and their variances are poorly known, the model predictions will be uncertain and difficult to use in decision-making. That shows the need to identify the key processes and to ensure that the parameter values associated with the key processes are well known. The committee notes that although this is not typically done, exposure models can be used to identify the most important fate processes for a given pesticide application. For example, Sato and Schnoor (1991) used EXAMS to study the fate of dieldrin delivered by runoff to an Iowa reservoir. The pesticide's fate was dominated by flushing and bed-water exchange, so dieldrin exposures were sensitive to the depth of the mixed bed, and getting that parameter right was necessary to achieve accurate modeling. Similarly, Seiber et al. (1986) found that volatilization of 2-methyl-4-chlorophenoxyacetic acid from rice fields did not result chiefly from water-to-air exchanges but rather from transfers of salts dried on foliage to the air. Such key chemical fate processes, once identified, are almost never pursued in sufficient detail to allow substantial improvement in exposure modeling. Although studies by pesticide registrants might yield useful site-specific information, the empirical observations do not typically yield generalizable understandings of fate processes that can be readily used in new situations without introduction of further uncertainty.

Finally, the committee notes that the pesticide fate and transport models do not provide information on the watershed scale; they are intended only to predict pesticide concentrations in bodies of water at the edge of a field on which a pesticide was applied. Different hydrodynamic models are required to predict how pesticide loadings immediately below a field are propagated through a watershed or how inputs from multiple fields (or multiple applica-

tions) aggregate throughout a watershed. Watershed-scale models, such as the Soil and Water Assessment Tool (SWAT), have been developed to predict the effects of agronomic practices on water and sediment. SWAT operates on a daily time step and can perform simulations over a long time (30 years) by using physical landscape characteristics (including soil types and topography), data on land cover and land use, weather data, and physical-chemical properties of compounds to simulate processes that dictate routing of water and sediment. The primary routes for chemicals to enter water from a site of application in SWAT are surface runoff and infiltration of applied chemicals into groundwater that can reach surface waters through lateral flow and recharge. Thus, SWAT has an interface with PRZM/EXAMS or the Groundwater Loading Effects of Agricultural Management Systems (GLEAMS) (Leonard et al. 1989; Knisel and Davis 2000) model and can be used to predict chemical concentrations at particular points in a watershed over variable intervals.

GEOSPATIAL DATA FOR HABITAT DELINEATION AND EXPOSURE MODELING

Geospatial data are critical for exposure modeling and for describing species' habitats. The committee was asked to consider what constitutes authoritative geospatial data. The following sections discuss the delineation of habitat, describe the criteria for authoritative geospatial data, and provide several examples of various types of authoritative geospatial data.

Characterization and Delineation of Habitat

Habitat refers to the abiotic and biotic environmental attributes in an area that allow an organism to survive and reproduce (Hall et al. 1997). Habitat configuration, area, and quality—which vary over space and time—affect probabilities of persistence of populations and species. Because habitat by definition supports survival and reproduction, the term *suitable habitat* is redundant, and the term *unsuitable habitat* is contradictory. Habitat is species-specific, although a specific abiotic or biotic attribute might be a habitat component for multiple species; habitat is not synonymous with land cover, vegetation, or vegetation structure (Hall et al. 1997). Detailed explanations and discussions of the concept of habitat are included in Fretwell (1972), Morrison and Hall (2002), and Mitchell (2005). Characterization and delineation of species' habitats is necessary to estimate where and when a given pesticide and a given species might co-occur, to make spatially and temporally explicit calculations of pesticide exposure, and to specify the spatial structure of population models used in effects analyses.

The first step in delineating habitat is to compile data on species occurrence and, ideally, data on species' demography and environmental attributes that are associated with occurrence and measured in the field. Numerous publications have compared methods for identifying and statistically modeling asso-

ciations between a species and its environment and have described the data requirements and the information content and potential applications of results (Scott et al. 2002; Elith et al. 2006; Franklin 2009; Royle et al. 2012). For example, resource-selection functions (Boyce et al. 2002; Manly et al. 2010) and occupancy models (MacKenzie et al. 2006) are among the diverse statistical methods that characterize habitat quality by relating data on the distribution or demography of a species to abiotic and biotic attributes of its environment. Regardless of method, the size of a species' range, and the specificity of its resource requirements, greater access to and reliability of geospatial data have made it easier to delineate and characterize habitat and habitat quality for a given species in space and time. The data also have improved the ability to model chemical fate and potential exposure of organisms. Horning et al. (2010) have presented a comprehensive, easily understood review of data sources and methods for application of remotely sensed data (data on an environmental feature that are not collected by physical contact with the feature) to ecological analyses.

Many caveats are associated with projections of habitat location and distributions of species. For example, most models of species distributions describe a statistical relationship between detections of an organism and elements of its habitat. The models tend to assume implicitly that species-environment relationships are stable—an assumption that might not be valid if habitat is currently unoccupied (Wiens et al. 2009) or if climate, land cover, or land use change (Araújo and Pearson 2005; Sinclair et al. 2010). Moreover, models of species distributions do not allow one to project species occurrence reliably in areas or periods in which environmental conditions are unsampled or otherwise unknown. Uncertainties increase if environmental data and species data were not collected in the same locations or during the same period. In addition, correlative models of species distributions do not account for phenotypic plasticity and adaptive evolution and therefore might overestimate reductions in range size in response to environmental change (Pearson and Dawson 2003; Skelly et al. 2007; Schwartz 2012).²

The level of uncertainty associated with a species' range and distribution and with delineation of its habitat is strongly affected by uncertainty in the data on species occurrence.³ Ideally, data on occurrence are gathered over many years, in many locations that span the range of values of major environmental gradients, and with a sampling design that reflects the biology of the species.

²*Phenotypic plasticity* is defined as modifications of behavior, appearance, or physiology of individuals in response to environmental change, and *adaptive evolution* is defined as heritable genetic changes that affect individual phenotypes and increase probabilities of population or species persistence.

³*Range* is defined as the total extent of the area occupied by a species or the geographic limits within which it occurs, and *distribution* is defined as the areas in which a species is projected to occur on the basis of modeled associations with environmental attributes.

Such data might be collected during a sponsored research project but otherwise can be relatively rare. It often might be necessary to rely on such data sources as the North American Breeding Bird Survey, the Biodiversity Informatics Facility maintained by the Center for Biodiversity and Conservation of the American Museum of Natural History, and records on threatened or nonnative invasive species maintained by NatureServe (a nonprofit organization that represents an international network of data centers and state-level natural heritage programs). A number of uncertainties are common to atlases or databases of species occurrence (Franklin 2009), but they might represent the best data available in the absence of recent, standardized, or comprehensive field data on occurrence. Provided that uncertainties are estimated, statistical characterization and delineation of habitat is generally objective and quantitative and is more reliable than qualitative and subjective descriptions of habitat. In the event that decision-makers consider the uncertainties to be so high that new information must be collected, much guidance (Noon 1981; Buckland et al. 2001; MacKenzie et al. 2006; Willson and Gibbons 2009; Samways et al. 2010) is available about practical sampling methods for different taxonomic groups.

Criteria for Authoritative Geospatial Data and Metadata

The reliability of habitat delineations and ecological risk assessment is increased substantially by use of authoritative geospatial information and data (henceforth geospatial data) in which all parties have confidence and that all agree to use. Use of the same geospatial data by government agencies, nongovernment organizations, and private companies could facilitate joint fact-finding—a process through which diverse and sometimes adversarial parties collaborate to identify, define, and answer scientific questions that inform policy development (Karl et al. 2007).

Authoritative geospatial data should meet three criteria: they should be available from a widely recognized and respected source; they should be publicly available, whether freely or for purchase; and, for applications in the United States, they should be accompanied by metadata consistent with the standards of the National Spatial Data Infrastructure (NSDI). The criteria are applicable regardless of the scale of the data. Metadata document the fundamental attributes of data, such as who collected the data, when and where the data were collected, what variables were measured, how and in what units measurements were taken, and the coordinate system used to identify locations. Metadata allow one to understand a data source in sufficient detail to replicate the data collection and determine whether the data are applicable to a given analysis or decision-making process. The Federal Geographic Data Committee (FGDC 2012) and Dublin Core (DCMI 2012) maintain detailed technical and nontechnical explanations of metadata. Different federal agencies and research consortia have developed metadata standards that differ somewhat but remain consistent with the NSDI standards.

Standardized systems of data organization, storage, and retrieval facilitate compilation, discovery, accessibility, and assessment of the enormous amount of data on the arrangement and attributes of geospatial features and phenomena on Earth. The infrastructure of the NSDI includes the materials, technology, and people necessary to acquire, process, store, and distribute geospatial data to meet diverse needs (NRC 1993). Because the NSDI includes standards for geospatial data and specifications for metadata, all data in the archive are compatible regardless of source (FGDC 2007). The NSDI is administered by FGDC, an organization of federal geospatial professionals and constituents whose objective is to ensure that data can be efficiently shared among users and meet readily available standards.

Among the types of geospatial data most useful for delineating habitat and estimating exposure and effects of pesticides on listed species and their ecosystems are those on topography, hydrography, meteorology, solar radiation, soils, geology, and land cover. Although those data are not mutually exclusive, they generally are represented with different spatial-data layers. The sections that follow describe the various types of geospatial data and provide several examples of authoritative sources of them. In many cases, there are multiple authoritative sources of each type of data on different spatial and temporal scales. Although it would be ideal to be able to identify specific authoritative sources, no one authoritative data source will be best for all habitat delineations, exposure analyses, or other applications. However, accuracy assessments of authoritative data sources that are generally available might allow one to gauge which source is likely to be the most reliable for a particular objective. For example, the accuracy of a certain land-cover class might have higher priority than the accuracy of other classes, depending on the species or pesticide.

Topographic Data

Topographic metrics (such as slope, aspect, and elevation) often represent environmental features that are closely associated with species distributions (Osborne et al. 2001; Clevenger et al. 2002; Shriner et al. 2002) and that can affect chemical fate and transport. Diverse algorithms and modules within Geographic Information System software, such as ArcGIS modules (Environmental Systems Research Institute, Inc., Redlands, California), are available for modeling topography (Pelletier 2008; Horning et al. 2010).

Topographic features, such as heterogeneity of elevation in a given area or the boundaries of watersheds, can be derived from digital data on elevation. Sources of free elevation data include the National Elevation Dataset, the Shuttle Radar Topography Mission, and the Global Digital Elevation Map. Digital elevation models are available at resolutions of 30 m, 10 m, and, in some areas, 3 m.

Two free modules for ArcGIS—Topography Tools (ESRI 2010) and DEM Surface Tools (Jenness Enterprises 2011)—allow derivation of topographic data. For example, Topographic Position Index measures whether the elevation of a

given pixel is greater or smaller than that of surrounding pixels. That information can be translated into values of slope that, in turn, can be used to model species-environment relationships (Dickson and Beier 2007). Topography also may be correlated with land uses, such as agriculture, residential development, and recreation.

Three-dimensional data acquired from light detection and ranging (lidar)—an optical remote sensing technology—afford many new ways to characterize vegetation, especially understory vegetation beneath tree canopies (Vierling et al. 2008), and to map the location and topography of flood plains and channels. ArcGIS modules, such as LIDAR Analyst (Overwatch Systems LTD 2009), enable processing and use of lidar data for developing accurate models of land-surface features at spatial resolutions relevant to many modeling applications (for example, less than one to tens of meters). Models of elevation and above-ground measures of vegetation structure derived from lidar data are increasingly used to model species' habitats and distributions (Bradbury et al. 2005; Martinuzzi et al. 2009). The US Geological Survey (USGS) Center for LIDAR Information Coordination and Knowledge is intended to improve access to lidar data and coordination among and education of its users (USGS 2012a).

Hydrographic Data

Watershed features are relevant to habitat delineation of terrestrial and aquatic species and to assessment of potential pesticide exposure of these species. For example, there might be fewer natural barriers to movements of species and toxicants along river banks and within watersheds than between watersheds. A national system of hydrologic unit codes (HUCs) divides the United States into six nested sets of watersheds; that is, large watersheds are progressively divided into smaller watersheds (Seaber et al. 1987). At its coarsest resolution, the HUC system delineates 21 regions that are large watersheds (such as the Rio Grande) or logical groups of similar drainages (such as the Pacific Northwest, California). Each region is labeled with a name and a two-digit number; for example, the Columbia River Basin is numbered 17. As HUCs are subdivided, each subdivision is labeled with a name and an additional two digits; for example, the combined Kootenai, Pend Oreille, and Spokane river basins correspond to number 1701, and the Kootenai River Basin is numbered 170101. The smallest hydrologic units, subwatersheds, have 12-digit labels (Table 3-1). Hydrologic units span nearly 5 orders of magnitude in size, from about 100 km² (40 mi²) for subwatersheds to about 460,000 km² (178,000 mi²) for regions. In some parts of the country, watersheds have been delineated at resolutions as fine as 16-digit HUCs (NRCS 2012a).

The standardized watershed boundaries of the HUC system provide a common geographic context for all users. The boundaries are available from USGS on paper maps (USGS 2010a) or in digital form (USGS 2012b). The metadata for the digital data and a description of the philosophical foundation of

the system also are available at no cost (USGS/USDA/NRCS 2011). Overlaying hydrographic and topographic data sometimes reveals inaccuracies in the geographic locations of small streams, but these inaccuracies typically can be resolved with aerial photographs or field validation.

Substantial amounts of data associated with six-digit HUCs are available on-line from EPA (2012e). The data are diverse and include social variables, such as human demography, and ecological variables, such as water quality. Data are provided in formats and with documentation that do not require substantial technical expertise to understand or apply.

Some states maintain an accounting system for water resources separate from the federal HUC system. For example, the Washington Department of Ecology defines water resource inventory areas (WA Department of Ecology 2012). The boundaries of the inventory areas are not identical with those defined by the HUC system, but the inventory areas have some historical precedent in the state. A map of the inventory areas also serves as a graphical user interface to access many types of data associated with the biology and management of listed species (WA Department of Ecology 2012).

After defining a watershed, one can classify the relative size and location of its constituent streams (Ritter et al. 2011). In this classification system, the smallest tributaries are assigned the order of 1 and referred to as first-order streams. When two first-order streams join, they continue as a single stream of the second order. When two second-order streams join, they form a single third-order stream, and so forth. Low-order streams (small numbers) are always in headwater regions, whereas high-order streams are main rivers. Stream ordering is not highly amenable to quantitative analysis because its application depends on the resolution at which an observer perceives the landscape. Small maps showing large areas, for example, might omit first-order streams that are apparent in field observations.

TABLE 3-1 Nested Hierarchy of Hydrologic Units

Number Digits in HUC ^a	Hydrologic Unit Name	Number of Units	Average Size of Unit in km ² (mi ²)
2	Region	21	459,878 (177,560)
4	Subregion	222	43,512 (16,800)
6	Accounting unit ^b	352	27,454 (10,600)
8	Cataloging unit ^b	2,150	1,813 (700)
10	Watershed ^c	~20,000	588 (227)
12	Subwatershed ^c	~100,000	104 (40)

^aHydrologic unit code.

^bNumbers of units and boundaries revised from Seaber et al. (1987) by later users.

^cMapping not yet complete.

Source: Seaber et al. 1987, later revised and reported by USGS 2011.

Meteorological Data

Variation in weather at relatively small spatial resolutions (such as kilometers to tens of kilometers) and temporal resolutions (such as days to a few years) can affect the distributions and population dynamics of organisms and their resources. Chemical fate and transport also are affected by meteorological variables, such as temperature, precipitation, and wind speed and direction. Accordingly, those variables will affect chemical-fate model parameters, such as probability of runoff and loads of suspended solids.

Meteorological data in the United States are archived and made freely available by national and regional centers maintained by NOAA. The National Climatic Data Center has complete data on the 122 primary National Weather Service (NWS) reporting stations in the United States.⁴ Gridded climatic data are also available for a variety of cell sizes (ESRL 2012). The six regional climate data centers provide the same data as the national center and observations or estimates of regional relevance (NCDC 2012). The meteorological data available through the national and regional sources are authoritative in that they were collected by the NWS or its partners, have been screened and checked by experts, are accompanied by complete metadata, and are publicly available. The data are available in tabular format and in a spatial format that meets the NSDI standards.

Solar Wavelength and Radiation Data

Solar radiation at wavelengths of about 290–600 nm affects rates of photochemical excitation and transformations and therefore chemical decomposition of pesticides. Data on solar radiation are used to calculate insolation—the amount of solar radiation that reaches a given location on Earth's surface—which affects cyclic or seasonal phenomena, such as migration; rates of growth and development; and the distributions of species in space and time.

Daily data on the distribution of solar wavelengths from the ultraviolet to the near infrared are available from the National Aeronautics and Space Administration Earth Observing System's Solar Radiation and Climate Experiment.⁵ However, the measurements of incoming solar radiation are taken at the top of the atmosphere rather than at Earth's surface. The distribution of wavelengths received at Earth's surface are a function of latitude, day of the year, time of day, slope and aspect of the surface, cloud cover, concentrations of aerosols in the atmosphere, and horizon obstruction (Rich et al. 1994). Therefore, without surface measurements, calculation of direct photolysis rates and half-lives of chemicals in water and on soil surfaces requires estimation of numerous atmospheric parameters and use of those parameters and spatial coordinates, time of

⁴See www.ncdc.noaa.gov/oa/ncdc.html.

⁵See <http://lasp.colorado.edu/sorce/>.

year, and time of day in a computer model, such as GCSOLAR (EPA 2012f) or SMARTS (NREL 2012). It might not be feasible to implement such models for all pesticides. Thus, existing geospatial data might not be sufficient to model some aspects of chemical fate. However, applying a model, such as SMARTS, to a given region and period (for example, the Pacific Northwest in spring) might allow one to determine the variability of the light intensity at the relevant wavelengths—those at which a given compound has high absorptivity. If exposure analysis suggests that photolysis is highly relevant to chemical fate, characterizing that variability would probably be valuable.

Insolation is calculated on the basis of Julian day and the coordinates and slope of the surface. ArcTools (ESRI, Redlands, California) also offers multiple tools for computing insolation for polygons or points. The Solar Radiation Graphics tool in ArcTools allows one to visualize the visible sky, the sun's position in the sky over time, and the sectors of the sky that affect the amount of incoming solar radiation, all of which are incorporated into calculations. The Photovoltaic Education Network provides an on-line calculator,⁶ which is authoritative in that it is a product of an organization that provides training for the solar engineering industry, its calculations are freely available, and the metadata provided on the site explain how the calculations are derived.

Soils Data

Soil type is associated with habitat quality for wild plants and agricultural crops and for animals that communicate by pheromones and other chemicals. Chemical fate might be associated with soil infiltration and runoff, and soil pH and anion-cation exchange capacities of soils are useful parameters for modeling sorption.

In the United States, the authoritative source for soils data is the Natural Resources Conservation Service (NRCS; formerly the US Soil Conservation Service) of the US Department of Agriculture (USDA). Since the 1930s, NRCS has mapped almost all the soils in agricultural areas in the country. Soils data are available as digitized maps accompanied by narrative descriptions and some numerical data about the soils (NRCS 2012b). Because almost all the original soil surveys were conducted at the county level, the data are organized by county. The base maps typically are aerial photographs on which polygons that represent different soil types are superimposed. Each soil type has a distinct identifier. Soil classification is conducted by interpreting aerial photographs and field surveys. The resolution of the resulting maps is sufficient to identify the soil type in individual fields.

The narrative for each county's soils contains quantitative information about particle sizes, basic soil chemistry, organic content, and hydrologic attributes. The narratives also describe soil horizons, which are multiple layers of soil

⁶See pvcddrom.pveducation.org/SUNLIGHT/MODTILT.HTM.

below the surface. Field measures of soil properties might be necessary for some model applications, but the NRCS soil surveys typically are adequate for models that require values of basic soil attributes. The NRCS soils data are authoritative in that they are products of USDA and the work of experts in soil science. The data are freely available and meet NSDI standards, and metadata are complete.

Geological Data

Geology strongly influences the chemistry of surface materials and shallow groundwaters that interact with pesticides. Authoritative geospatial data on geology in the United States are provided by USGS via its Mineral Resources Online Spatial Data (USGS 2012c) and to a lesser extent by the offices of state geologists or state geological surveys. For example, Washington state provides geospatial geological data on the distribution of rock units, including rock types and the geological age of each unit (Dragovich et al. 2002). Further information about the physical characteristics of each rock unit is published by USGS or its state counterparts.

The geology of the entire United States has been mapped on some scale. In most cases, geological maps are available at the resolution of counties; in some areas, the map scales are as fine as 1:24,000. USGS maintains a Web site with an interactive map of the United States that is linked to geological data on each state in a variety of formats (USGS 2012c). The site also links to complete metadata for each state, publications that describe the methods used to generate geological maps, and narrative descriptions of the physical and chemical properties of surface and subsurface rocks. Geospatial data on geology were collected to support numerous activities, such as mineral exploration, detection of faults, oil and gas exploration, and designation of national parks. As a result, there is considerable variation in the supporting documentation and narrative descriptions of the maps.

Nationwide geological data reflect more than a century of detailed mapping and analysis by expert geologists. The metadata are extensive, data and narratives are freely available, and the maps adhere to the standards of the NSDI.

Land-Cover Data

Land cover encompasses both natural features—such as native vegetation, rock formations, and bodies of water—and features produced by human activity, such as agricultural fields and urban areas. Types and quantities of pesticides applied sometimes can be inferred on the basis of the distribution of crop types. Delineating habitat for some species or assessing particular exposures might not be possible on the basis of existing classifications of land cover. Depending on the species biology or the pesticide characteristics, it might be necessary to develop a new classification of regional land cover on the basis of satellite images,

aerial photographs, and field validation. For example, although the boundaries of agricultural fields might be stable over many years, crop types might vary among and within years. When a time series of land-cover data is available, it might be possible to develop a spatially explicit probability distribution of changes in all or a subset of land-cover types. Features of agricultural land that might be attributes of habitat for some species, such as small groups of trees or streams, typically are not included in publicly available crop data. However, in many cases, it is sufficient to derive land-cover data from another source. Whether a new classification is necessary depends on the target location, species, and pesticides; the focus of the assessment, which will determine the relevant cover types and spatial and temporal scale of the data needed; and the necessary level of data accuracy.

USGS provides numerous sets of land-cover data that cover the conterminous United States and smaller areas, such as selected states or ecosystems (USGS 2010b). More detailed data are available on some land-cover types, such as wetlands and forests. Among the most commonly used sets of land-cover data derived from Landsat images at 30-m resolution are the National Land Cover Dataset and those available from the National Gap Analysis Program (Scott et al. 1993, 2002) and the Landscape Fire and Resource Management Planning Tools (LANDFIRE) project. Regional programs, such as the Southwest Regional Gap Analysis Project, offer seamless maps—which do not change abruptly at state boundaries—of land cover across multiple states with climate and species composition that are distinct from elsewhere in the nation. Both national and regional gap-analysis programs provide projections of the current ranges and distributions of multiple taxonomic groups. For example, the national program includes range data on 1,376 species of amphibians, birds, mammals, and reptiles and distribution data on 810 species (USGS 2011).

The National Agricultural Statistics Service provides spatial data and metadata on the distribution of 133 classes of land cover, including major crop types, across the country (NASS 2010). Principal sources of raw data for its classification are the Resourcesat-1 Advanced Wide Field Sensor and Landsat Thematic Mapper. National data are available on each year since 2008; data on 2011 are at 30-m resolution. Annual data on some states extend back to 1997. The Web-based application CropScape (Han et al. 2012) is a user-friendly interface with the data.

State and local sources of spatial data on agricultural land use vary. For example, since 1984, the California Farmland Mapping and Monitoring Program has tracked the distribution of agricultural land and urban development (CA Department of Conservation 2007a). The program releases spatial data every 2 years with a minimum mapping unit of 4 hectares. Data sources include aerial photographs, public comments, and field surveys. Among the land-use classes are grazing land, urbanized land, four types of farmland, and five types of rural land (CA Department of Conservation 2007b).

UNCERTAINTIES IN EXPOSURE MODELING AND PARAMETER INPUTS

The chemical-fate models with such diverse information as geospatial data can be used to obtain an EEC. Many uncertainties are associated with that estimation, and this section explores some of the most important ones and suggests methods for addressing them.

Pesticides and Mixtures

The first requirement for successful exposure modeling involves identification of the specific substances that are to be introduced into the environmental setting. Those data are needed not only to evaluate exposures to individual components but to assess prospective interactions of the components. To have an informed discussion on pesticide exposure, three types of mixtures need to be distinguished.

Pesticide formulations. Typically, a pesticide manufacturer or supplier mixes one or more active ingredients—the chemicals that are responsible for a pesticide's biological effects—and other chemicals. The mixture is what is often referred to simply as the pesticide or the pesticide formulation. The committee notes that virtually no chemical is synthesized as a pure compound, so impurities occur in the synthesis of the pesticide active ingredients. Although manufacturing processes try to reduce the number and concentrations of impurities, technical-grade active ingredients that are used to make the pesticide formulations will contain the active ingredients and some impurities.

Tank mixtures. In most pesticide applications, pesticide formulations are added to a tank or other container with adjuvants (see below). The term *tank mixture* refers to the material in a tank or container at the time that the material is applied to a treatment area, such as an agricultural field. Exposure issues associated with pesticide formulations and tank mixtures share a property that greatly simplifies exposure analysis—the materials are applied at the same time to a defined location. More important, the identity and concentration of the constituents are known.

Environmental mixtures. This term is used to designate all contaminants that are in the environmental media of concern, such as water in the case of salmonids. Environmental mixtures are the results of previous applications of tank mixtures—sometimes many tank mixtures applied at different times to different areas in a watershed or other locale of concern. In addition, environmental mixtures include other environmental contaminants not related to pesticide applications in the media of concern. Because environmental mixtures are the results of many sources of contamination, estimating the components in environmental mixtures quantitatively is far more difficult than estimating exposures associated with the application of a single tank mixture.

For pesticide risk assessments, EPA typically focuses its assessments on the active ingredients, whereas the Services contend that all the other chemicals or whole products need to be considered. The following sections describe in further detail the types of mixtures potentially involved, their components, and difficulties encountered in incorporating them into an exposure analysis.

Pesticide Formulations and Tank Mixtures

Pesticide formulations typically contain chemicals other than the active ingredients that often do not have a direct effect on the target species. The term *inert* is used to designate a chemical that is not classified as an active ingredient. Some inerts can be toxic, and EPA has proposed the term *other ingredients* rather than *inerts* (EPA 2012g). Nonetheless, *inert* is engrained as a term in the pesticide literature and is commonly used—for example, the EPA Inert Ingredient Assessment Branch, which was established in 2005. For brevity, the following discussion uses the term *inert* but recognizes that inerts might be biologically active and potentially hazardous.

The term *adjuvant* is closely related. Adjuvants differ from inerts only in that adjuvants are added to a tank mixture in the field at the time that the pesticide is applied rather than when it is formulated. Tank-mixture adjuvants—such as surfactants, compatibility agents, antifoaming agents, spray colorants (dyes), and drift-control agents—are added to a tank mixture to aid or modify the action of a pesticide or the physical characteristics of the mixture (Ferrell et al. 2008).

Inerts and adjuvants are an extremely broad array of chemicals, including carriers, stabilizers, sticking agents, and other materials added to facilitate handling or application. Mixtures of different pesticide formulations or pesticide formulations in combination with various adjuvants are typically applied to save time and labor and to reduce equipment and application costs. Such a mixture might also control a variety of pests or enhance the control of one or a few pests.

EPA is responsible for the regulation of inerts and adjuvants in pesticide formulations. EPA (52 Fed. Reg. 13305 [1987]) developed four classes (lists) of inerts on the basis of the available toxicity information: toxic (List 1), potentially toxic (List 2), unclassifiable (List 3), and nontoxic (List 4). List 4 was subdivided into two categories: List 4A contained inerts on which there was sufficient information to warrant a minimal concern, and List 4B contained inerts the use patterns of which and toxicity data on which indicated that their use as inerts was not likely to pose a risk. Although EPA no longer actively maintains the lists, references to that classification system are in the older literature; moreover, EPA documents, such as the current Label Review Manual (EPA 2010), still refer to the lists of inerts.

After a review of the toxicity data that supported food tolerances for pesticide inerts, EPA (71 Fed. Reg. 45415[2006]) revoked food tolerances for over 100 inerts; that is, these inerts can no longer be used in pesticides that are applied to food commodities. Thus, no List 1 inerts are now allowed in food-use

pesticide formulations. Only five of the original 50 List 1 inerts—di-*n*-octyl adipate; ethylene glycol monoethyl ether; 1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester; 1,4-benzenediol; and nonylphenol—are now permitted in non-food-use pesticide formulations (EPA 2011). In 2011, EPA released a searchable on-line database of inerts that are approved for use in pesticide formulations (EPA 2012h). The database includes three sets of inert ingredients: those approved for food and nonfood use, for nonfood use only, and for fragrance use.

Some inerts used in pesticide formulations are complex mixtures, for example, petroleum-based solvents and tallow-based surfactants. Petroleum hydrocarbon solvents can contain many individual compounds, and the compositions of the solvents vary substantially, depending on the distillation process and on the sources and types of the crude oil used to derive the petroleum distillates (ATSDR 1999). Similarly, surfactants based on tallow (animal fat) are highly complex mixtures whose compositions vary on the basis of the source of the animal fat and the manufacturing processes used to render the animal fat and process the tallow (Kosswig 1994; Brausch and Smith 2007; Katagi 2008).

In some cases, applications of multiple pesticide formulations and tank mixtures might not present difficulties in the exposure analysis beyond those associated with applications of a single compound. If components of a tank mixture or formulation do not substantially affect the fate and transport of other components, the exposure analysis methods used for single chemicals can be applied to tank mixtures. In cases in which additives, such as surfactants, could affect the fate and transport of active ingredients in a formulation, uncertainties in exposure analysis could be substantial unless the effect of additives can be quantified in exposure modeling. Many inerts are designed to affect the behavior of an active ingredient after application. For example, surfactants or penetrating agents are often used in applications of herbicides. Surfactants and penetrating agents might have little or no phytotoxicity at the concentrations used in most herbicide applications, but their ability to enhance absorption can enhance the efficacy of herbicides (Denis and Delrot 1997; Liu 2004; Tu and Randall 2005). Surfactants can also alter the persistence and mobility of active ingredients in soil and water (Katagi 2008); similarly, microencapsulation can retard transport in soil. Prolonging residence time can enhance the efficacy of pesticide active ingredients in soil (Beestman 1996).

The environmental-fate properties of inerts often differ from the corresponding properties of a pesticide's active ingredients. Consequently, inerts and active ingredients partition differentially in the environment (water, sediment, soil, and air) and do so at differing rates. Individual constituents in complex inerts also have different environmental-fate properties, so components of the inerts also partition at different rates and to different extents. Little information is available on the environment fate and differential partitioning of complex inerts. Although a relatively standard set of tests are required on the environmental fate of most active ingredients, testing requirements are less stringent for inerts.

Environmental Mixtures

Unless exposure occurs only at or near the point of pesticide application, species are more likely to be exposed to environmental mixtures than to a single pesticide formulation or tank mixture. Environmental mixtures are formed when a tank mixture—active ingredients, inerts, and adjuvants—combines with other chemicals that are already present in the environment from other sources, such as other pesticides from previous applications and pharmaceutical, consumer, and personal-care products in municipal effluent.

As a formulation or tank mixture moves away from the initial point of application, its components often do so at different rates and exhibit differential partitioning into various environmental media (surface soil, surface water, sediment, and air) and undergo transformations—for example, fipronil to its more toxic and persistent degradates (Lin et al. 2009)—at different rates. The chemical components become diluted in environmental media that already contain other chemicals, including pesticides. For example, in Oregon's Willamette River Basin, only 3.6% of surface-water samples collected during 1994-2010 contained only a single detected chemical; over 50 pesticide mixtures of two to six pesticides each were found in the remaining samples (Hope 2012). Nationally, more than 6,000 unique mixtures of five pesticides were detected in agricultural streams (Gilliom et al. 2007). The data from Gilliom et al. (2007) are cited in the BiOps (NMFS 2008, 2009, 2010) as a basis for documenting that exposures to environmental mixtures will occur. The monitoring data from Gilliom et al. (2007), however, are not associated with specific applications of pesticides.

Approaches to estimating exposures to environmental mixtures are at least conceptually similar to those associated with pesticide formulations or tank mixtures. If the exposure factors are known—that is, the pesticide and environmental components, their concentrations, and their locations at a specific time—exposure-analysis methods can be used to assess exposures to the environmental mixture. In practice, however, quantitative estimates of exposures to environmental mixtures are seldom feasible owing to the dynamic state of the environmental mixtures and the varying compositions of the mixtures over space and time. In any given location or watershed, the amounts of pesticide active ingredients, inerts, and adjuvants in environmental media will be highly variable and depend on pesticide use and other sources of environmental contamination.

As noted by the Services, the EPA pesticide risk assessments do not directly or explicitly incorporate information on exposures to environmental mixtures. The Services commonly address environmental mixtures in the assessment of the *baseline* (the state of a population excluding exposure to the pesticide under consideration), but these considerations are largely qualitative rather than quantitative. Although all the BiOps discuss available modeled estimates and monitoring data on multiple pesticides that might occur as environmental mixtures (see, for example, NMFS 2011, Table 107), this information is not used

quantitatively to modify risk assessments that focus on exposure to one or more active ingredients. NMFS (2011, p. 442) notes that "given the complexity and scale of this action, we are unable to accurately define exposure distributions for the chemical stressors." Essentially the same language is included elsewhere (NMFS 2008, p. 259; 2009, p. 309; 2010, pp. 449-450).

The qualitative discussions of exposures to environmental mixtures in BiOps by the Services and the focus of EPA on single chemicals are not fundamentally different. EPA's basic agreement with the position taken by NMFS is clearly illustrated in its response to questions posed by the committee (EPA 2012i, p. 5), which included the following:

The highly variable nature of the background exposure to other chemical stressors represents a significant impediment to combined effects analysis. Much of the empirical data for multiple chemical stressor evaluation involves small suites of chemicals, in discrete concentration combinations that are not highly representative of in-field conditions across complex landscapes at the national scale of pesticide use that EPA must assess. In addition, predicting the frequency and pattern of environmental mixtures at the temporal scales used in acute and chronic risk assessment (hours to a few weeks) is beyond the capabilities of the best available nationwide data sets that look at combined chemical analysis.

The statements by EPA and NMFS above are functionally identical with respect to the qualitative rather than quantitative treatment of environmental mixtures.

The Services (see, for example, NMFS 2008, 2009, 2010, 2011) and other analysts (for example, Hoogeweg et al. 2011) often discuss or assess the potential co-occurrence of various pesticides (that is, pesticide active ingredients) with populations of listed species, but quantitative analyses of the co-occurrence of multiple pesticides have not been encountered in EPA assessments. As discussed in Gilliom et al. (2007, p. 81), an analysis of the co-occurrence of pesticides might be useful in identifying environmental mixtures that have the greatest probability of adversely affecting listed species, and these investigators provide a preliminary assessment of the most commonly occurring mixtures of two to seven pesticides (Belden et al. 2007). More detailed analyses of the frequency of the co-occurrence of pesticides have been used in human health risk assessments (e.g., Stackelberg et al. 2009; Tornero-Velez et al. 2012). The preliminary analyses by Belden et al. (2007) on pesticides associated with corn and soybean production suggest that factoring the occurrence of environmental mixtures into assessments will increase the risk estimates but not substantially (by a factor of about 2). Although some BiOps (NMFS 2008, 2009, 2010) cite the analysis by Belden et al. (2007), they do not attempt to model exposures to multiple pesticides in a single watershed.

Pesticide Application Rates

Pesticide application rate is another important source of uncertainty. Despite a label's explicit application specifications, such as 1 lb of material per acre for corn fields, users commonly apply lower quantities according to the severity of their weed or pest infestation. However, Steps 1 and 2 of the ESA process (Figure 2-1) should ensure that no potentially unsafe pesticide applications are ignored. Accordingly, an exposure modeler can only assume that a given pesticide is applied at the maximum allowable rate. Furthermore, in Step 3 of the process (Figure 2-1), the Services cannot reasonably be expected to use information that suggests that substantially lower application rates are used unless supporting data are available. Such data must include statistical descriptions of the spatially and temporally distributed application rates. Moreover, some measures would have to be taken to ensure that a use pattern could not dramatically increase in any particular season or locale (for example, because of crop shifts). Only then could exposure modelers use such knowledge to obtain EECs with associated uncertainties. For now, pesticide use is probably an inaccurate input for exposure analysis; registration and labeling are not well suited for solving this exposure-analysis bias.

Other Fate-Modeling Parameters

Even if release rates per unit area of all the pesticide components were well quantified, other phenomena add uncertainty to estimates of exposure of various environmental surfaces, such as plant surfaces, soil surfaces, and surface water. For example, AgDRIFT includes numerous and diverse parameters (see Box 3-1). The certainty with which each relevant parameter for a particular pesticide application is known will influence the certainty of estimated chemical loadings on foliage, soil surfaces, and even neighboring surface waters. Bird et al. (2002) compared field data with AgDRIFT model evaluations for "161 separate trials of typical agriculture aerial applications under a wide range of application and meteorological conditions." The comparisons all relied on case-specific meteorological data (wind, temperature, and humidity) and application data, such as observed aircraft heights and nozzle equipment. With such inputs, the investigators concluded that the "model tended to overpredict deposition rates relative to the field data for far-field distances, particularly under evaporative conditions" by about a factor of 3. However, the AgDRIFT estimates were in good agreement (to within less than a factor of 2) with "field results for estimating near-field buffer zones needed to manage human, crop, livestock, and ecological exposure." Overall, aggregating the data for the various application methods resulted in ratios of model predictions to field measures of $10^{-0.03 \pm 0.5}$ at 23 m and $10^{0.10 \pm 0.9}$ at 305 m, given as $10^{\text{mean} \pm \text{SD}}$, where SD is standard deviation. Therefore, despite simplifying assumptions and the variability of some of

the input parameters, one might conclude that the model itself operates fairly accurately. Bird et al. (2002) concluded that "the model appears satisfactory for regulatory evaluations." However, greater uncertainty in the output of the model will arise when it is applied as a general screening tool and case-specific input parameters, such as wind speeds and mode of application, are not known. That situation is true for other complex models, such as PRZM/EXAMS. One option for improving the situation is to use relevant geospatial data for estimating relevant fate-modeling parameters and their variability.

In addition to inaccuracies and imprecisions in initial pesticide loadings on soil, parameters used in chemical-fate models, such as PRZM and EXAMS, have associated uncertainties, particularly because pesticides often contain or are applied with other chemicals that can affect some fate processes. Data sources for assigning values to parameters range from empirical observations reported by pesticide registrants to information extracted from peer-reviewed journal publications that sought to elucidate underlying process mechanisms. As illustrations, consider two processes that are typically important in chemical-fate modeling: sorption and biodegradation. Both have been studied intensively for decades.

BOX 3-1 AgDRIFT Inputs

Aircraft information	Spray-material information
Aircraft type (fixed-wing, biplane, helicopter)	Tank-mix specific gravity
Aircraft semispan or rotor radius	Tank-mix flow rate
Spraying speed	Tank-mix nonvolatile fraction
Rotor-blade RPM (helicopter)	Tank-mix active fraction
Aircraft weight	Evaporation rate
Propeller Information	Meteorological information
Aircraft drag coefficient	Wind speed
Aircraft platform area	Height of wind-speed measurement
Engine efficiency	Surface roughness
Propeller RPM	Wind direction
Propeller-blade radius	Wet-bulb temperature depression (temperature and relative humidity)
Propeller location	
Nozzle information	Other information
Number of nozzles	Spraying height
Nozzle type	Number of swaths
Nozzle locations	Swath width
Drop size distribution	Swath displacement

Source: Teske et al. 2002.

Sorption phenomena are generally well understood, and sorption coefficients can be estimated relatively well in many cases. Assuming application of the correct sorption model (see below), sorption inputs in pesticide-fate models probably have only a moderate uncertainty (a factor of 3). For example, sorption coefficients (K_d values) can typically be estimated for nonionic organic compounds by using the product, $f_{oc}K_{oc}$, in which f_{oc} is the organic carbon content of the soil or sediment ($\text{kg}_{oc}/\text{kg}_{solid}$) and K_{oc} is the organic carbon-normalized sorption coefficient ($\text{mol kg}^{-1}_{oc} / \text{mol L}^{-1}_{water}$). In a review of the literature, Gerstl (1990) found that K_{oc} values for atrazine are log-normally distributed and vary only by about a factor of 2 (± 1 SD) for 217 reported measurements of atrazine (Figure 3-1; $K_{oc} = 10^{2.1 \pm 0.3}$ given as $10^{\text{mean} \pm 1 \text{ SD}}$). That result is similar to the factor of 2.5 found by Seth et al. (1999) and suggested in the EXAMS user manual. It is also consistent with observations reported by Novak et al. (1997) for atrazine sorption in a single field site (Figure 3-2). Consequently, the sorption coefficient, K_d ($\text{L}/\text{kg}_{solid}$) for a specific soil or sediment, calculated by using the f_{oc} of that solid, can be known almost as precisely as the pesticide's K_{oc} values because site-specific f_{oc} measures can be made with great precision. However, if model calculations use a generic value for f_{oc} or even a value based on regional soil mapping (see section "Geospatial Data for Habitat Delineation and Exposure Modeling" above), one can readily anticipate deriving another factor of 2 from "real-world" variability around the f_{oc} term used to make the K_d estimate.

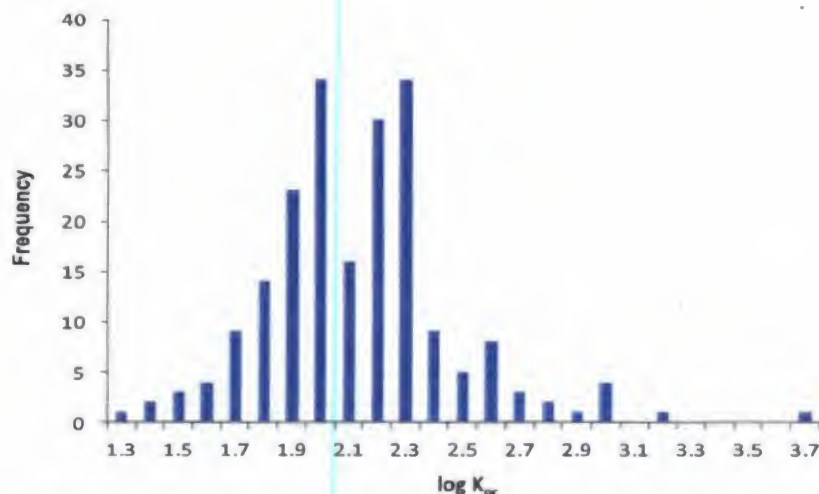


FIGURE 3-1 Organic-carbon normalized sorption coefficients, K_{oc} , values for atrazine plotted on a logarithmic scale. Source: Gerstl 1990. Reprinted with permission; copyright 1990, *Journal of Contaminant Hydrology*.

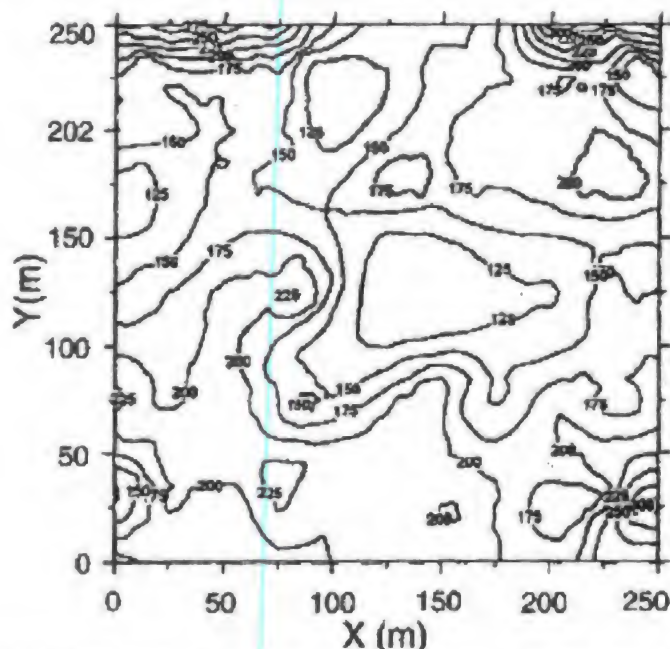


FIGURE 3-2 Distribution of K_{oc} values for atrazine in a 6.25 hectare field, showing a range of about a factor of 2. Source: Novak et al. 1997. Reprinted with permission; copyright 1997, *Journal of Environmental Quality*.

Perhaps more important, larger inaccuracies in predicting the amount of chemical sorbed to soil or sediment particles will result if the model used to describe the sorption process is inaccurate. For example, one cannot expect an accurate result if one uses a sorption model designed for nonionic pesticides ($K_d = f_{oc}K_{oc}$) when modeling ionic compounds. Some modelers made that mistake with the herbicide 2,4-D, which typically exists in water as a negatively charged species. A modeler should expect its sorption to involve anion exchange, as has been shown by Hyun and Lee (2005). A second case of an inappropriate use of the $f_{oc}K_{oc}$ model involves situations in which black carbon sorbents play an important role in addition to the rest of the organic carbon. Yang and Sheng (2003) have provided evidence of such sorption to black carbon in the case of diuron applied to a field with burned wheat and rice residues. Thus, although cases that accurately use the $f_{oc}K_{oc}$ model probably reflect modest levels of uncertainty (1 SD, reflecting a factor of 2-4), pesticide-fate modelers should recognize both chemical-specific properties and site-specific conditions that can cause their estimates of sorption to be quite inaccurate—not merely imprecise but biased by a factor of 10—when such a sorption model is inappropriately used (Accardi-Dey and Gschwend 2002).

Even the best estimates of biodegradation coefficients are generally much more uncertain than sorption estimates. When Laskowski (1995) reviewed literature on biodegradation rates in soils, he found that for many chemicals few soils were tested (Table 3-2). However, when substantial data were available, biodegradation rates varied widely, often by more than a factor of 10 (Table 3-2). Likewise, Paris et al. (1981) found that the rates of biohydrolysis of the butoxyethyl ester of 2,4-D varied by up to a factor of 25 in 33 water samples tested even when efforts were made to account for sample-to-sample variations in microbial population densities. Finally, in some cases, such as nitrilotriacetate, Tiedje and Mason (1974) observed significant lag periods (4-6 days) in three of 11 soils tested. Thus, inaccuracies will result if a simple first-order removal-rate law with a single-value rate coefficient is used for periods that are shorter than or comparable with such lag periods.

TABLE 3-2 Variability of Pesticide Degradation Rates in Soils

Pesticide	No. Soils Tested	Ratio of Highest to Lowest Degradation Rate Observed	Reference
Nitrilotriacetate	11	80	Tiedje and Mason 1974
Crotoxyphos	3	36	Konrad and Chesters 1969
Carbofuran	4	25	Getzin 1973
Glyphosate	4	19	Rueppel et al. 1977
Flumetsulam	21	10	Lehmann et al. 1992
Chlorimuron ethyl	19	8	L.M. Kennard and D.A. Laskowski, DowElanco, unpublished material, 1992
Thionazin	4	7	Getzin and Rosefield 1966
Nitrapyrin	10	6	Laskowski and Regoli 1972
Imazaquin	3	5	Basham and Lavy 1987
Chlorsulfuron	8	4	Walker et al. 1989
Methidathion	4	3	Getzin 1970
Aldicarb	2	2	Richey et al. 1977
Diazinon	4	2	Getzin and Rosefield 1966
Linuron	4	2	Lode 1967
Methomyl	2	2	Harvey and Pease 1973
Propyzamide	5	2	Walker 1976

Source: Adapted from Laskowski et al. 1982; Laskowski 1995.

In the few cases in which sufficient data are available, it appears that biodegradation rates are log-normally distributed (Figure 3-3). For example, the (pseudo-) first-order rate coefficients reported by Lehmann et al. (1992) for flumetsulam appear to have a log-normal distribution (Figure 3-3, $N = 21$). Paris et al. (1981) also found that the microbial population-normalized rate coefficients appeared to be log-normally distributed with a k_{bio} value of about $10^{0.7 \pm 0.3}$ L/colony forming units (cfu) per hour ($10^{\text{mean} \pm \text{1SD}}$, $N = 33$) for biohydrolysis of the butoxyethyl ester of 2,4-D. In both cases, the data suggest uncertainty of about a factor of 2 (about ± 0.3 log units around the mean). To summarize, pesticide-exposure analysis should be pursued by using enough biotransformation information to establish whether the rates are normally or log-normally distributed, and then the data should be analyzed to obtain the mean rate coefficient and its variance for use in fate modeling.

It is also clear that rates of biodegradation of some pesticides can vary widely as a function of site conditions. As stated by Howard (1991) in discussing 2,4-D in surface waters,

the rate will depend on a number of factors including presence of acclimated organisms, nutrient levels, temperature and concentration of 2,4-D. Half-lives in river water of 18 to over 50 days (clear water) and 10 to 25 days (muddy water) with lag times of 6 to 12 days have been reported.... Degradation is poor in oligotrophic water and where high 2,4-D concentrations are present and 2,4-D was not mineralized in water from 2 or 3 lakes tested.

Clearly, environmental conditions (such as temperature and oxic or anoxic conditions in soil or sediment), nutrient availability, and factors controlling pesticide speciation (dissolved vs sorbed) can greatly affect biodegradation. Perhaps the general uncertainty in biodegradation rates is best captured in the tendency of some investigators to refer simply to individual pesticides as "non-persistent," "moderately persistent," and "highly persistent." For example, Corbin et al. (2004) describe 2,4-D as "non-persistent" ($t_{1/2} = 6.2$ days) in terrestrial environments, "moderately persistent" ($t_{1/2} = 45$ days) in aerobic aquatic environments, and "highly persistent" ($t_{1/2} = 231$ days) in anaerobic terrestrial and aquatic systems.

An Example of Current Modeling Input Choices in the Face of Parameter Uncertainty

To understand the approaches being used to account for uncertainty in modeling parameters, one can consider how biodegradation information was used in a PRZM-EXAM analysis of the ethyl hexyl ester (EHE) of 2,4-D (see Table 3-3). The compound is a nonionic ester, is quite hydrophobic, and thus is

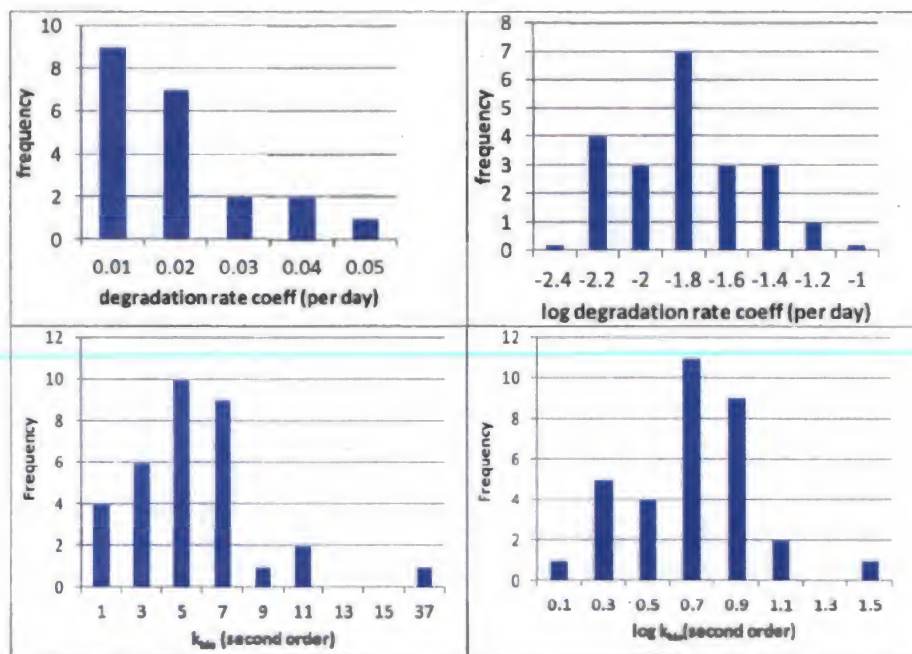


FIGURE 3-3 Upper panels: Distribution of observed (pseudo-) first-order biodegradation rates (per day) of flumetsulam as reported for 21 test soils by Lehman et al. (1992) on linear (left) and logarithmic (right) scales. Lower panels: Distribution of observed bacterial-number-normalized biodegradation rates (L/organism-hour) of the butoxyethyl ester of 2,4-D as reported for 33 test surface waters by Paris et al. (1981) on linear (left) and logarithmic (right) scales.

highly sorptive (K_{oc} about 10,500). In a typical soil with an organic carbon content near 1%, one expects a sorption coefficient near 100 L/kg. That value means that almost all the ester (over 99%) is sorbed and somewhat unavailable to microorganisms. The extensive sorption implies that soil-to-soil differences in organic carbon content will affect the ester's bioavailability correspondingly and change the biodegradation rate accordingly. For example, soil with 3% organic carbon content will limit this ester's bioavailability by a factor of 3 relative to soil with 1% organic carbon content.

Next, the aerobic soil metabolism rate listed in Table 3-3 is based on a single soil-volatility study in which the ester was seen to degrade with a half-life of 8 days. Clearly, that information is not enough to provide any sense of the statistical variability in the biodegradation rate. Consequently, Corbin et al. (2004) compensated by providing some margin of safety, cutting the rate by a factor of 3 to arrive at a half-life of 24 days in aerobic soil. However, no scientific justification for a factor of 3 is provided; such a choice would require more observations. Furthermore, as directed in the modeling guidance (see Footnote b of Table 3-3), the aerobic aquatic degradation rate was set to half the value used for the aerobic soil case, yielding a half-life of 48 days. In the absence of any data, the guidance also leads one to assume that the ethylhexyl ester of 2,4-D is "stable" in anaerobic medias, such as sediments. Given those somewhat arbitrary inputs, PRZM/EXAM proceeds to estimate environmental concentrations of 2,4-D EHE. The approach leaves no possibility of assessing the probability distributions of the resultant EECs. The outcome of the model is quantitative, but its accuracy and precision are unknown.

Quantifying Parameter Uncertainty

It is clear from the above discussion that input parameters for fate and transport models have several components of uncertainty, including differences associated with environmental variability, imprecision of measurements under natural conditions, and lack of knowledge (see Chapter 2). Therefore, use of single values in a deterministic modeling approach provides an unwarranted sense of accuracy in predicting pesticide fate and later concentrations in water or loading on sediments and soils. As discussed in Chapter 2, the committee recommends taking a probabilistic approach and assigning appropriate distributions to the input parameters instead of single values. The committee notes that EPA has been working on probabilistic exposure modeling for many years (see, for example, Burns 2001). Model runs can be done with Monte Carlo techniques as single-level or multilevel models. The output is then a range of possible environmental concentrations with their associated probabilities of occurrence. That approach provides the required input information for comparison with hazard function to provide a probabilistic risk estimate.

TABLE 3-3 Biodegradation Rate Coefficients and Other Physical-Chemical Data Used in PRZM/EXAMS Fate Modeling of the Ethylhexyl Ester of 2,4-D

Model Parameter	Value	Comments	Source
Aerobic soil metabolism, $t_{1/2}$	24 days ^a	Estimated upper 90th percentile	MRID 42059601
Aerobic aquatic degradation, $t_{1/2}$ (KBACW)	48 days	Half the aerobic soil metabolism degradation rate	Estimated per EFED Guidance ^b
Anaerobic aquatic degradation, $t_{1/2}$ (KBACS)	Stable	No data	Estimated per EFED Guidance ²
Aqueous photolysis, $t_{1/2}$	128 days		MRID 42749702
Hydrolysis, $t_{1/2}$	48 days		MRID 42735401
K_{oc}	10,500 ml/g		Estimated by EpiSuite Software
Molecular weight	333.26		Product Chemistry
Water solubility	0.32 mg/L		Product Chemistry
Vapor pressure	4.57 E-6 mm Hg		Product Chemistry
Henry's law constant	5.78 E-5 atm-m ³ /mole		Product Chemistry

^aThree times (upper 90th percentile) based on single soil half-life estimated from acceptable laboratory volatility study of 8 days.

^bFrom *Guidance for Chemistry and Management Practice Input Parameters for Use in Modeling the Environmental Fate and Transport of Pesticides*, dated February 28, 2002. Abbreviations: EFED, Environmental Fate and Effects Division of EPA; KBACS, first-order rate constant for pesticide's bacterial degradation in sediment (day⁻¹); KBACW, first-order rate constant for pesticide's bacterial degradation in water (day⁻¹); MRID, master record identification number (a unique cataloging number assigned to an individual pesticide study at the time of its submission to the agency).

Source: Corbin et al. 2004.

Interdependence of Input Parameters

Intervariable dependence can result in large uncertainty in model output, particularly when probabilistic modeling techniques are used. Assuming that all variables in an assessment are mutually independent will lead to erroneous risk results that might be conservative. That situation occurs whether the distributions characterizing the several variables represent natural variability or lack of information. Correctly modeling dependences usually requires additional empirical information beyond means, dispersions, and marginal distributions of input

parameters and requires special modeling and mathematical techniques to propagate dependence. It seems unlikely that all input parameters are independent or perfectly dependent; these are the cases for which relatively simple solutions exist. However, the complexities of modeling incomplete dependence of multiple model parameters (Ferson et al. 2004; Kurowicka and Cooke 2006) probably outweigh the increased precision of the models. Therefore, for regulatory purposes, including ESA consultations, the committee recommends continuing to use the simplifying assumption of independence of model input parameters and to acknowledge the residual uncertainties of such an approach.

CONCLUSIONS AND RECOMMENDATIONS

Exposure-Modeling Practices

- Although the mass-balance models have many strengths, model limitations need to be recognized, and the appropriate model needs to be used for different risk-assessment contexts. Accordingly, a screening-level model should not be used when a refined exposure analysis is needed, such as in Step 2 or 3 assessments in the ESA process.
- To estimate pesticide exposure concentrations at various stages, the committee proposes a stepwise approach to exposure modeling. Step 1 would determine whether a pesticide and listed species overlap geographically and temporally. Step 2 would first identify the most important fate processes and other related considerations and then simplify the pesticide-fate model to estimate time-varying and space-varying pesticide concentrations in generic habitats relevant to the listed species. Step 3 would use refined models and the regional-specific or site-specific input values relevant to the listed species.
- Field studies need to be distinguished from general monitoring studies that are not associated with specific pesticide applications under well-described conditions. The latter cannot be used to estimate pesticide concentrations after a pesticide application or to evaluate model performance.
- Model predications are only as accurate or precise as parameter information. Thus, key processes need to be identified and the associated parameter values well defined.

Geospatial Data

- Although data on species occurrence inevitably are incomplete, uncertainties in modeled distributions of species typically can be quantified, and statistical characterizations of species distributions, species-environment relations, and the location and quality of habitat are more objective and reliable than qualitative descriptions of habitat.

- Existing and authoritative geospatial data on many scales are sufficient to support a substantial majority of habitat delineations and exposure analyses under the ESA and FIFRA. Widely recognized sources of data on environmental attributes—including topography, hydrography, meteorology, solar radiation, soils, geology, and land cover—can be used reliably for modeling species distributions and chemical fate. The authoritative sources that are most useful will vary among species and pesticides.
- Use of data and metadata that comply with the National Spatial Data Infrastructure can increase the clarity and repeatability of data analysis; facilitate quantification or even reduction of uncertainties in analytical results; and improve communication.

Uncertainties

- Any exposure analysis involving pesticide applications should at least qualitatively describe the potential effect of inerts on the environmental fate of an active ingredient. If the available information suggests that inerts (or adjuvants) might substantially affect the fate or transport of an active ingredient, the effect should be assessed quantitatively if data to support such a consideration are available.
- The extent to which the environmental fate of inerts or adjuvants needs to be considered quantitatively will depend largely on toxicological considerations (see Chapter 4). In the absence of information on the environmental-fate properties of inerts or adjuvants, quantitative structure-activity relationships can be used to estimate fate properties, but the use of such estimates will add to the uncertainties in the exposure analysis.
- Ideally, any risk assessment or BiOp should be based on exposures to pesticide components and other chemical agents that will occur in the field. Nonetheless, few methods are available for assessing exposure to environmental mixtures quantitatively or for predicting the relative concentrations of different mixture components in various environmental media, especially water and sediments. Monitoring data on the pesticides and other stressors will provide information about what is occurring in a specific area of concern but are not useful for model comparisons.
- In the absence of quantitative estimates of exposure, assessors should exclude potential mixture components from quantitative assessments. Uncertainties associated with the identities or exposure concentrations of potential mixture constituents should be qualitatively described to a decision-maker.
- Many diverse parameters are used in chemical-fate models, and their accuracy is important ultimately for the concentrations estimated in modeling efforts. However, little effort has been expended to evaluate the data inputs relevant to particular ESA evaluations. Therefore, if the agencies want to obtain more accurate modeling results, a subset of case-specific exposure estimates

should be evaluated by pursuing a measurement campaign specifically coordinated with several pesticide field applications.

- Sorption and biodegradation are important chemical-fate processes that are often associated with substantial uncertainty or represented inaccurately in fate models. More sorption data are needed to characterize nonlinear isotherms over concentration ranges and under conditions that are applicable to relevant agricultural settings, such as pH, ionic composition, and solid-phase mineralogy. Likewise, more data are needed to determine biodegradation coefficients, whether biodegradation rates are normally or log-normally distributed, and under which circumstances lag periods are important.

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4

Effects

As discussed in Chapter 1, pesticides are designed to have biological activity and are "intended for preventing, destroying, repelling or mitigating any pest" [7 U.S.C. § 136 (u)(1)]. Pesticides might cause a variety of effects on non-target organisms, including listed species, and effects on individuals might ultimately affect a population. Determining the potential for and possible magnitude of effects is a process known as effects analysis, and various aspects of that process are addressed in this chapter.

First, the committee discusses characterization and evaluation of sublethal, indirect, and cumulative effects. Next, it describes the models that are used to estimate effects of a pesticide at the individual and population levels, clarifies the relationship between the models at these two levels, and evaluates major assumptions used in the modeling approaches.

Because there are many sources of uncertainty in effects analysis, the final three sections of this chapter address various aspects of uncertainty. As described in Chapter 3, pesticides are typically mixtures (formulations) of active ingredients and other materials (inerts), are often mixed with other pesticides and other chemicals (adjuvants) in the field, and are applied to areas that already contain mixtures of chemicals. What is evaluated becomes a complicated question and is often viewed as a substantial source of uncertainty. Accordingly, the committee discusses the state of the science of mixtures assessment and provides some guidelines on assessing the hazard posed by a pesticide active ingredient in light of all the other components in the formulation, tank mixture, and environment. It then addresses the uncertainty surrounding interspecies extrapolations and the use of surrogate species and the quantitative characterization of uncertainty.

Throughout this chapter, the committee provides suggestions on how to incorporate the information presented into the approaches used by the US Environmental Protection Agency (EPA) to determine whether a pesticide "may affect" (Step 1, Figure 2-1) or is "likely to adversely affect" a listed species (Step 2, Figure 2-1) and into the approaches used by the US Fish and Wildlife Service

(FWS) and the National Marine Fisheries Service (NMFS)—collectively referred to as the Services—to make jeopardy determinations (Step 3, Figure 2-1).

SUBLETHAL, INDIRECT, AND CUMULATIVE EFFECTS

Pesticides can kill organisms that are closely or distantly related to their intended targets, and they can cause sublethal changes that can affect reproduction, shorten lifespans, or make the organisms unable to compete. The following sections discuss how to incorporate sublethal effects into ecological risk assessments, how effects on one organism might indirectly affect others, and how pesticide effects might be modified by exposure to other environmental stressors.

Sublethal Effects

Pesticides can have sublethal effects at multiple levels of biological organization: molecular, cellular, tissue, organism, population, and community. Only when compensatory or adaptive mechanisms at one level of biological organization begin to fail do deleterious effects become apparent at higher levels. The committee considered how to assess objectively the degree to which observed effects of pesticides on organisms are *adverse*. Defining that concept is essential for ecological risk assessment because even if an effect is reliably observed, that alone might not be sufficient to conclude that the effect is adverse. The committee concluded that the only reasonable way to determine whether an effect is adverse and how adverse it might be is to assess the degree to which it affects the organism's survival and reproductive success. It then is possible to extrapolate from changes in an individual organism's survival or reproductive success to estimate population effects. If an adverse effect is large enough, it might lead to extinction of the species. EPA reached a similar conclusion in its overview of the ecological risk-assessment process (EPA 2004, p. 31): "If the effects on the survival and reproduction of individuals are limited, it is assumed that the risk at the population level from such effects will be of minor consequence. However, as the risk of reductions in survival and/or reproduction rates increase, the greater the potential risk to populations."

EPA and the Services agree on the inclusion of sublethal effects in the risk-assessment process but disagree on the extent to which such effects should be included. For example, in its responses to committee questions, EPA explained that its focus is "on how to relate the relevance of sublethal data to an assessment of the risks to fitness of listed species," with *fitness* defined as "an individual's ability to survive and reproduce" (EPA 2012a, p. 2). Furthermore, EPA considers that incorporation of sublethal effects into an ecological risk assessment must be accompanied by an explicit relationship that defines the contribution of the sublethal effect to an individual organism's fitness in terms of the end points of "survival, growth and reproduction" (EPA 2012a, p. 20). EPA

stated that it “does not believe that all sub-lethal effects or that all levels of a sub-lethal effect on an individual constitute a compromise of individual fitness” (EPA 2012a, p. 3).

EPA’s approach differs from the Services’ approach. For example, FWS “casts a wide net for each potentially affected species to ensure that the most sensitive endpoints are captured and evaluated” (FWS 2012, p. 2). It contends that “at present, data describing ‘sub-lethal’ effects are acknowledged but then set aside and not used by EPA in making effects determinations or characterizing the potential effects of the action, unless other data or studies are available that would enable EPA to quantify a relationship between the ‘sub-lethal’ effect and EPA’s traditional endpoints, survival, growth, or reproduction.” FWS (2012, pp. 2-3) continued that “in contrast, when characterizing the ‘Effects of the Action’ pursuant to the ESA [Endangered Species Act], the FWS does not limit itself to using only those data that quantify changes in survival, growth, or reproduction.”

As discussed in the section on effects models below, assessing the effects of pesticides on listed species requires quantifying the effect of a pesticide on survival and reproduction of a species in the wild. Any effect that results in a change in one component is relevant to the assessment. In contrast, any effect that does not change either component is irrelevant with respect to a quantitative assessment of population effects. The relevance of any particular sublethal effect is likely to depend on the species. Growth, for example, might be a relevant effect in some species but not in others. In mammalian species, retarded growth might increase age of first reproduction but not affect reproductive output thereafter. In many fish species, size of the individual organism is directly related to reproductive output throughout the lifespan. Many plant species do not need to achieve a particular size for maximal reproductive output. Therefore, the committee recommends that EPA in Step 2 (see Figure 2-1) cast a wide net and identify information about sublethal effects of a chemical. If possible, EPA’s assessment should include information about responses at various chemical concentrations (a concentration-response curve) and, at a minimum, include a qualitative assessment of the relationship between sublethal effects and survival and reproduction. In Step 3 (see Figure 2-1), the Services should show how such effects change demographic measures (survival or reproduction) of a listed species and incorporate such information into the population viability analyses or should state that such relationships are unknown but possible and include a qualitative discussion in the uncertainty section of the biological opinion (BiOp). The Services face the greatest challenge in Step 3 in determining whether an observed sublethal effect will change survival or reproduction in the natural population and, if so, the magnitude of such a change in relation to the predicted exposure.

Relationships between sublethal effects and changes in population growth rates span a continuum of uncertainty that depends on the ability to quantify the

link. At one extreme, the relationship between a sublethal effect and survival or reproduction has not been quantified empirically, and the available mechanistic information is not sufficient to model the causal chain quantitatively. For example, markers of oxidative stress—such as glutathione or superoxide dismutase—indicate a physiological response to a chemical, but the relationship of the response to survival or reproduction is not known. Such a response could not be easily quantified with respect to population assessment if the observed response were the only pertinent information.

At the other extreme, the link between sublethal effects and population persistence might be clear, quantifiable, and well documented in the literature. For example, the singing ability of some male birds directly affects the probability of their establishing and holding a territory and forming pair bonds with mates (Spencer et al. 2003). Impaired singing ability could directly affect reproductive success during the breeding season if the male song did not attract a female mate. Similarly, impaired growth of juvenile salmon might result in a reduction in size of individual salmon as they migrate to sea and could reduce survival. Specifically, Baldwin et al. (2009) modeled the relationship between sublethal effects on acetylcholinesterase activity and feeding behavior of juvenile Chinook salmon and reductions in growth after short-term exposure to environmentally realistic concentrations of organophosphate and carbamate pesticides. Reductions in growth correlated with reduced size at ocean entry and with later survival. Mebane and Arthaud (2010) modeled the effects of sublethal effects of low concentrations of copper on growth of juvenile Chinook salmon and projected potential effects on population size, recovery rates, and extinction risks.

Many sublethal effects might have a link to population viability, but that link has not yet been quantified. An example is altered olfactory ability, which has been shown to increase predation risk in some species of salmon because of an inability to detect chemical cues that signal the presence of a predator or because of a loss of homing ability (Scholz et al. 2000). Whether altered olfactory ability affects survival will depend on the degree of its expression in the natural environment, the presence of predators during the time that olfaction is lost, and whether it occurs in fish whose size makes them susceptible to predation. Impaired immune function is another example in which an organism is affected, but the effect on population viability is unclear. A working immune system is critical for survival, but an alteration of some aspect of immune function and its effect on disease resistance are often less clear—for example, Does a given reduction in circulating leukocytes affect susceptibility to disease? Furthermore, the effect of an impaired immune system on disease susceptibility hinges partly on the presence of a pathogen. The committee notes that exposure to pesticides in some species might actually increase defense responses to predation. For example, Barry (1998) observed increased helmet formation—a defense response that deters predation efficiency—in daphnia exposed to low concentrations of endosulfan.

Exposure

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Uncertainties in concentration-response relationships or differences between laboratory and field responses, particularly behavioral responses, further complicate the quantification of changes in survival and reproductive success in response to sublethal toxicity. Assessment of sublethal effects, as well as cumulative and indirect effects, is even more complicated in species that have complex life cycles and population structures, such as Pacific salmon (see Box 4-1 for further discussion).

The committee concludes that survival and reproduction are the principal effects in determining population viability. The inability to quantify the relationship between sublethal effects and survival or reproductive success does not negate the potential importance of such effects for population persistence. However, the relationship remains a hypothesis that can be described only qualitatively with reference to the scientific literature for why such a hypothesis is tenable. Implications for risk characterization can be discussed qualitatively, not quantitatively, as an additional uncertainty beyond uncertainties that are propagated in a formal quantitative manner. The narrative can be considered by a decision-maker according to the applicable policy constraints regarding risk tolerance. However, such a separation of important risk components and uncertainty into quantitative and qualitative portions that cannot formally be combined makes it difficult to integrate and interpret the results of a risk assessment. Integration can be improved by quantifying better the relationships that are viewed as critical for understanding the risks posed by a pesticide to a listed species. One way to facilitate integration of the hypothetical relationship into the formal risk assessment is to conduct extensive reviews of comparative data or empirical case studies or to conduct targeted new studies that could help to derive defensible scientific quantification of the links between sublethal effects and survival or reproduction.

Indirect Effects

The Services have defined *indirect effects* as "those that are caused by the proposed action and are later in time, but still are reasonably certain to occur" (50 C.F.R. 402.02). Thus, their definition from a regulatory standpoint characterizes indirect effects as simply delayed effects. Depending on how one interprets that definition, it could be quite restrictive and different from most ecologists' understanding of indirect effects, which typically include effects on prey, competitors, or predators of a listed species or on other aspects of the species' ecological milieu but not direct effects on the species. On the basis of the documents reviewed by the committee, it appears that the restrictive definition is not used by the agencies; therefore, this section discusses indirect effects as including those normally understood by the term.

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BOX 4-1 Ecological Risk Assessment in Species That Have Complex Population Structure and Life History: Pacific Salmon and Trout

Pacific salmon and trout (*Oncorhynchus* spp.) are the basis of valuable commercial and recreational fisheries; part of the economy, ceremony, and subsistence of American Indians; components of complex ecosystems to which they contribute great quantities of nutrients; symbols of clean water and healthy rivers; and a host of other attributes related to human and natural systems (NRC 1996). Many factors have contributed to declines in salmon and trout, which are, in some cases, protected under the US Endangered Species Act (Gustafson et al. 2007). Protection of the listed distinct population segments (DPSs) has ramifications for a wide variety of human activities, including application of chemicals to control animals and plants that are considered crop pests and weeds.

There are five species of Pacific salmon in North America: Chinook, *O. tshawytscha*; coho, *O. kisutch*; sockeye, *O. nerka*; chum, *O. keta*; and pink, *O. gorbuscha*. There are also two trout species of the same genus: rainbow/steelhead trout, *O. mykiss*, and cutthroat trout, *O. clarkii*. Both trout species are quite variable phenotypically and have several subspecies (Behnke 1992). All Pacific salmon are spawned in freshwater, and most migrate to sea and return to freshwater at maturity to spawn (that is, they are anadromous); however, resident populations of sockeye salmon (kokanee) are well known and a few individuals of other salmon species (such as Chinook salmon) do not migrate to sea but mature to a small size in streams. All trout are spawned in freshwater, but may be exclusively nonanadromous or resident (that is, they spend their whole lives in freshwater), a mix of anadromous and resident, or virtually all anadromous. Each salmon and trout species is structured into discrete breeding populations because the adults return to their natal site to spawn (Quinn 2005). Therefore, the population, rather than the species, is the fundamental unit of conservation, and this is why DPSs of Pacific salmon and trout have been listed.

As a consequence of the complex population structure of Pacific salmon, some breeding populations can be highly endangered whereas other populations of the same species are abundant and able to sustain substantial exploitation from fisheries—for example, sockeye salmon in the Stanley Basin of Idaho vs those in Alaska's Bristol Bay (Hilborn et al. 2003; Gustafson et al. 2007). Pacific salmon and trout populations also vary considerably in life-history patterns, including the timing of a series of key events: the return migration by adults from the ocean to freshwater, the spawning season, the emergence of juveniles from gravel nests, the duration of residence in freshwater, and migration to sea (Quinn 2005). Therefore, depending on the species and populations in question, fish might be present in one river at vulnerable times of their lives and absent from another river at the same time of that year, and these variations in life-history traits could affect how salmonids are exposed to pesticides. For example, some juvenile Chinook salmon migrate from their natal streams to the ocean in their first summer of life whereas

other juveniles of the same species spend a full year in the river system before migrating to sea (Taylor 1990; Healey 1991). The committee notes that the variation in spatial and temporal distribution of juvenile salmon residing in and migrating from river systems is further complicated by the substantial numbers of hatchery-produced juveniles, whose differences from wild fish in size, growth rate, and release timing can all affect migration patterns (Giorgi et al. 1997; Beckman et al. 1998).

Sublethal effects on sensory capacity, reaction, swimming ability, buoyancy control, or other aspects of performance might increase mortality. For example, chlorpyrifos, a common organophosphate insecticide, inhibited acetylcholinesterase in the brain and muscle of salmonids and affected spontaneous swimming and feeding behaviors of juvenile coho salmon in a concentration-dependent manner in the laboratory (Sandahl et al. 2005). Whether and to what degree sublethal effects affect survival in natural conditions is not clear. Laboratory exposure of cutthroat trout to carbaryl, an insecticide applied to oyster beds in some estuaries, affected swimming performance and predator avoidance (Labenia et al. 2007). It is certainly plausible (and perhaps even parsimonious) to conclude that there will be effects on survival in natural settings if environmental concentrations and exposure durations are comparable with those in the laboratory experiments, but the magnitude of the effects in relation to other sources of mortality is difficult to measure or model. Another complication in modeling the effects of pesticide exposure is that salmonids often prey on other salmonids (Duffy and Beauchamp 2008).

Moreover, if the population as a whole is stressed by factors that increase mortality over natural levels—such as water diversions that reduce flows, dams that alter sediment transport patterns, shoreline development in rivers or estuaries, or predation by nonnative species—the cumulative effects of the many stressors might be sufficient to put populations in jeopardy even though any single stressor, such as pesticide exposure, could have been sustained. Chemicals can also have indirect effects on individual organisms and the population. For example, most of the diet of juvenile salmon and trout in streams consists of insects, both larval stages of aquatic insects and terrestrial insects that fall on the stream surface (Nielsen 1992). Reductions in the prey base by pesticides might affect growth rate and life-history transitions that depend on growth (Mangel and Satterthwaite 1998) and have subtle but profound effects on fitness. Analogously, shifts in the insect community and changes in fish behavior associated with fine sediment in the stream bottom might reduce growth and survival of juvenile steelhead (Suttle et al. 2004).

Finally, the variation in life-history traits, between and even within species and subspecies, reinforces the importance of knowing the ecology of the particular species and population of concern for ecological risk assessment. It also highlights the difficulty of identifying a reliable surrogate species for testing and analysis, in particular a species whose life history is similar to that of the species of interest. For example, pink salmon generally migrate the short distance to the sea as soon as they emerge as free-swimming fry whereas juvenile Chinook salmon usually remain in freshwater for months to a year

(Continued)

BOX 4-1 Continued

and coho for more than a year. Pink salmon usually spawn within a few kilometers or tens of kilometers of the sea whereas Chinook salmon can migrate 1,500 km upstream or more to spawn, so their juveniles have to migrate the same distance to return to the sea. The different species also have different preferences for spawning substrate, stream sizes, and spawning seasons, all of which vary among their geographic distributions. Thus, the choice of a surrogate species for analysis and testing is challenging and complex at best. Even more challenging are the intraspecific variations in behavior, physiology, and distribution. For example, stream-type and ocean-type Chinook salmon differ in many attributes (Quinn 2005) that could affect exposure and vulnerability to pesticides. All the variation further emphasizes the need to assess the suitability of the surrogates and the applicability of the laboratory tests carefully when making decisions about likely effects of pesticides and other chemicals on listed species (Macneale et al. 2010).

~~Pesticides can indirectly affect a given species via effects on other species in the community. Indirect-effects analysis examines how a pesticide affects the habitat of a species. Because the indirect effects of pesticides on the species of concern can be favorable or unfavorable, it is more appropriately described as effects analysis than as hazard analysis. For example, the prey of the species of interest might be reduced in abundance or eliminated by the pesticide, perhaps because the prey is the target pest species or is affected along with the species of interest. Alternatively, populations of its predator or competitor might be reduced and the abundance of the species of interest thereby increased.~~

Because some indirect effects can be quantified, the committee recommends that they be incorporated into effects analysis. For example, for a situation in which food is the limiting factor and the major indirect effect is a 50% reduction in the food resource of the species of interest, the indirect effect can be incorporated into the population model by a 50% reduction in carrying capacity (maximum population size that can be supported by a specified area). In most cases, determining and quantifying such effects are more challenging and might require a conceptual model that incorporates the major components and linkages of the species' habitat that would respond to pesticide applications (see section "Effects Models" below). The modeling would entail an understanding of the ecology of all the species that might be at risk from pesticide exposure that live in the same area as and use resources similar to those of the listed species. There might be multiple nodes and links between affected species and the species in question, which might result in a fairly complex community dynamics model.

There are many candidate models and associated computer software for simulating community and ecosystem interactions (see, for example, Verhoef and Morin 2010). The primary hurdle in their use in decision-making applications is the large number of parameters that are poorly known, which

results in substantial implicit uncertainty. Because of the uncertainty, it is important when using such modeling tools to strive to estimate component uncertainties quantitatively in a realistic and scientifically defensible way and to propagate all the component uncertainties through the community-level analysis formally and explicitly. Such methods as Bayesian networks and Monte Carlo approaches for quantifying uncertainty in analyses were discussed in Chapter 2. If quantitative information about community relationships is lacking, a qualitative modeling approach could be considered, such as signed digraphs, loop analysis, and matrix analysis (Puccia and Levins 1991). Those types of modeling can help to determine which variables should be included in a community or ecosystem model and can provide insight into which ones should be measured to provide the greatest reduction in uncertainty.

As in the different approaches used to evaluate sublethal effects, EPA and the Services appear to differ (on the basis of their responses to committee questions) in the extent to which they consider indirect effects. EPA (2012a, p. 22) stated that "if the best available biological information for a listed species does not establish a relationship between the affected taxa and the listed species, EPA believes that a no-effect conclusion is warranted." That approach is logical, but *relationship* is not defined. FWS (2012, p. 5) stated that EPA does not consider potentially important "tertiary" effects and that "community-level effects are not considered." FWS (2012, p. 5) continued that EPA "only considers potential direct effects to those resources immediately relevant to the listed species." Likewise, NMFS (2012, p. 4) stated that "aspects such as prey dynamics (e.g., how quickly prey availability returns to background levels) and trophic consequences of herbicide applications are not considered" by EPA.

EPA uses a chemocentric approach to the assessment and begins with what is known about a chemical and its potential to affect various attributes of species' habitat. The Services take a species-centric approach and describe what is known about the life history of the species of concern, from which they infer the potential for pesticide-related effects. The different approaches seem to follow the same pattern as those used to evaluate sublethal effects, in which EPA takes a more quantitative approach and the Services a more qualitative approach. However, both quantitative information and qualitative information are necessary for comprehensive ecological assessments of the interactions of xenobiotic chemicals with the critical features of a species' habitat. Development of a species-specific conceptual model during the problem-formulation phase of the ecological risk assessment includes a specific enumeration of the important habitat components, which can then be addressed quantitatively or qualitatively—depending on the available information—during the effects analysis. The FIFRA Endangered Species Task Force has already begun to gather information on habitat and niche requirements of endangered species into an electronic database accessible to EPA and the Services (FESTF 2012).

Cumulative Effects

In the context of the ESA, cumulative effects are defined as “those effects of future State or private activities, not involving Federal activities that are rea-

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as parasitism and predation, are more predictable and are density-dependent (they depend on the number of organisms present). Exposure to pesticides is one of many exogenous stressors that might influence the type and degree of response of species (Coors and De Meester 2008). Rohr et al. (2006) proposed using concepts in community ecology and evolutionary theory to provide insights about cumulative effects of pesticides and other anthropogenic or natural stressors. Their approach encompasses the use of direct and indirect effects of pesticide applications to assess the sensitivity of various communities and to identify which stressors will have the greatest effect.

The stressors that currently affect listed species are considered part of the environmental baseline conditions. Therefore, the interaction of existing stressors with the pesticides under consideration is within the purview of the Services and appropriately part of a BiOp. EPA, as the action agency, is responsible for providing the Services with any information that is known about how toxicity of a pesticide is modified by environmental factors (for example, effects of cold

stress on pesticide toxicity). The responses to multiple stressors that are likely to have an effect (or have an increased effect) in the future are the cumulative effects. The committee has concluded that population models (see section "Effects Models at the Population Level" below) provide an objective, quantitative, and practical framework for incorporating baseline conditions and projected future cumulative effects into the ecological risk assessment in a way that is relevant to the requirements of the ESA. For example, a population model can represent the direct effects estimated from concentration-response relationships as reductions from baseline in survival and reproductive success and also can include effects on survival and reproduction of current and future habitat loss (as decreasing carrying capacity), habitat fragmentation (as changes in the spatial structure of the model), and climate change (for example, as increases in temporal variability of survival and fecundity to simulate the effect of an increase in frequency of extreme weather events). Such an approach will necessarily be chemocentric because the pesticide is the additive stress, but the approach also takes into account species-environment interactions and includes the effects of stressors other than the pesticide on a species.

In some cases, the pesticide being assessed has been in use for a long time, and the baseline population model already includes pesticide-induced reductions in survival and fecundity. Therefore, the calculated reductions in survival and fecundity are added to the baseline model's survival and fecundity (thus increasing their values) to obtain a model that simulates the dynamics of a population that is not exposed to the pesticide. The difference between the projections of that model and of the baseline model is an estimate of the degree to which current use and past use of the pesticide are contributing to the risks faced by a listed species or preventing its recovery. Thus, the risk assessor uses the information (risks with and without the pesticide) to inform the reregistration decision. The procedure described here does not require any more data than the case in which the baseline data are coming from populations that are not exposed to a pesticide.

EFFECTS MODELS

Effects models are used to characterize the effects of a pesticide at the individual level (effects on survival and reproduction) and at the population level (effects on population viability and recovery). EPA and NMFS use different models to evaluate the potential effects of a pesticide active ingredient on listed species and critical habitat. As described in its overview of ecological risk assessments for listed species (EPA 2004), EPA does not use effects models in its assessments. It assesses direct effects associated with different pesticide concentrations by using a risk-quotient (RQ) model that involves dividing an estimated exposure concentration by an effect concentration based on various prescribed toxicity tests and on published data. The derived RQ is compared with various levels of concern (LOCs) to determine whether a direct effect is likely. During

its Step 2 assessments, EPA might also use direct-effect LOCs to draw inferences about the potential for indirect effects on listed species that rely on nonendangered organisms as critical food or shelter resources. The indirect-effects analysis also serves as the basis for analyzing potential effects on designated critical habitat. Population effects are addressed simply as an extension of individual effects; if survival or reproduction is affected, EPA assumes population-level consequences and makes a "likely to adversely affect" determination, which requires formal consultation with the Services (Step 3, see Figure 2-1). See Chapter 5 for further discussion of the RQ approach.

NMFS uses population models as one of several lines of evidence to address the question of population persistence explicitly. The BiOp on the effect of three pesticides on salmonids (NMFS 2008) served as an example of the NMFS modeling approach for the committee. In that BiOp, NMFS assessed risk by examining the overlap in the estimated environmental concentration (EEC) and effect concentration ranges, using a literature survey of effects observed in the field, and using a weight-of-evidence analysis for multiple lines of evidence applicable to a number of risk hypotheses. NMFS also evaluated potential effects of pesticides on populations with two models: a life-history population model that estimated changes in a population's rate of growth (λ) on the basis of reduced individual survival after a 4-day exposure to acutely lethal concentrations and an individual-based growth and life-history population model that also estimated changes in λ on the basis of reductions in growth of juveniles due to acetylcholinesterase inhibition and reduced prey abundances. That modeling was not done for a specific EEC but for a range of possible environmental concentrations that could be related to an EEC.

The committee was asked to consider the various approaches for evaluating pesticide effects, and it interpreted its specific task concerning models to be an assessment of modeling approaches at the individual and population levels, a clarification of the relationship between models at these two levels, and an evaluation of the major assumptions of the models. The following sections address those topics.

Effects Models at the Individual Level

All chemicals affect organisms through interactions at the cellular level—for example, binding to cell receptors and inducing or blocking normal responses, inhibiting or stimulating enzymes, causing cell death, or disrupting normal DNA replication. Some cellular changes result in measurable responses that might affect an organism's ability to survive and reproduce. Because organisms have redundant systems to maintain homeostasis and various mechanisms to detoxify and eliminate chemicals, there are exposures below which no organismal (individual) effects occur. However, individual organisms differ in their ability to tolerate chemical exposure, and this results in variability around the effects threshold. Variability throughout the toxic range is illustrated by a standard *con-*

centration-response curve (also known as a dose-response or exposure-response curve), which is essentially a cumulative distribution function of the percentage of animals in a test population that exhibit a given response at each exposure concentration.

Superimposed on the interindividual (intraspecies) biological variability is variability from different sources, including interspecies variability, and uncertainty resulting from measurement imprecision and from extrapolation of experimental concentrations. Those types of uncertainty and approaches to incorporating them in individual-level models are discussed below in the section "Interspecies Extrapolations and Surrogate Species." The combined effects of those types of uncertainty can be expressed as confidence intervals around values on the concentration-response curve.

To evaluate potential effects on a species correctly, direct effects of pesticides on survival and reproduction must be estimated, and these estimates must correspond to the conditions expected in nature. The range of concentrations needs to include all plausible values that might result from the fate and transport models (see Chapter 3) for the populations that are being assessed. Because the values vary in space and time, the predicted effects on survival and reproduction also vary. The temporal and spatial variability in direct effects must then be incorporated into the population model to estimate population-level effects. An important source of uncertainty in this process is the measurement of direct effects on individual survival and reproduction under laboratory conditions, where demographic rates might be higher than in the natural environment of the species. Thus, the results of laboratory experiments need to be scaled to values expected in nature. There are two aspects of that scaling. First, the effects measured in the laboratory must be used to estimate the toxicant's effects in nature by taking into account the relative periods of exposure in the laboratory experiments (P_e) and in the wild (P_w). That step is not necessary if the two exposure periods are about the same. However, if there is a substantial difference, an adjustment might be necessary. For example, if the experimental mortality (M_e) is measured over a 4-day period, but the exposure in the wild is estimated from exposure models to be, for example, 8 days, the overall mortality in the wild (M_w) might be higher than in the laboratory. How much higher depends on assumptions about how the pesticide affects individual organisms. An extreme assumption would be that all organisms that are highly responsive to the pesticide die in the first 4 days and that the mortality over 4-day and 8-day periods would be the same ($M_w = M_e$). Another assumption could be that mortality in the wild is the same during each 4-day period. Thus, pesticide mortality in the wild would be calculated as $M_w = 1 - (1 - M_e)^{P_w/P_e}$. Second, the estimated toxicant mortality must be combined with the natural mortality. For example, if pesticide mortality and natural mortality are independent, the survival rate in the natural environment of the species can be calculated as $(1 - M_w)(S)$, where S is the survival rate in nature without any pesticide effects. In some cases, the calculated mortality is expected to be in the baseline model because the pesticide has been in use and the model parameters are based on a population exposed to

the pesticide (see the section "Cumulative Effects" above). In that case, the survival rate in the model (S) already includes the calculated pesticide mortality (Mw). To obtain a model that simulates the dynamics of a population that is not exposed to the pesticide, the survival rate would be calculated as $S/(1 - Mw)$, again assuming that pesticide mortality and natural mortality are independent. Although the examples in this section are given only for mortality effects, similar calculations also need to be done for the reproductive component of the effects data.

The committee notes that the effects end point is often summarized as a single point on the concentration-response curve, such as the concentration that kills 50% of the test population (LC_{50}). However, for the purposes of population modeling as discussed below, the effects must be estimated at a range of concentrations that includes all values that the populations that are being assessed might plausibly experience. Therefore, the committee concludes that test results expressed only as threshold values or point estimates—for example, the no-observed-adverse-effect level, the lowest observed-adverse-effect level, or the LC_{50} —provide insufficient information for a population-level risk assessment.

Effects Models at the Population Level

The results of the effects model (the changes in survival and reproductive success as a function of pesticide exposure) are used in population models to assess effects on listed species. Population models are used to estimate population-level end points—such as population growth rate, probability of population survival (population viability), and probability of population recovery—on the basis of individual-level effects. Because the ESA is concerned with species or listed units within named species, the effects of pesticides must be expressed at the population and species levels. Therefore, the committee concludes that population models are necessary to quantify the effects of pesticides on populations of listed species.

The need for effects analyses to be conducted at the population level has been emphasized for at least the last 2 decades (see, for example, Cairns and Pratt 1993; Baird et al. 1996; Ferson et al. 1996; Munns et al. 1997; Forbes and Calow 1999) and has been covered in several recent books (see, for example, Pastorok et al. 2002; Akçakaya et al. 2008; Barnthouse et al. 2007; Stark 2012). The applications of population models for effects analyses are too many to list comprehensively; some examples are Munns et al. (1997), Kuhn et al. (2000), Topping et al. (2005), Duchet et al. (2010), Willson et al. (2012).

Other types of models that have been used to assess ecological risks posed by pesticides and other toxic chemicals include models of individual organisms, bioenergetics models, and community and ecosystem models. As noted, the focus on population models in this report is necessitated by the specific requirement of predicting effects on listed species (for example, the risk of extinction) under the ESA. Other modeling types are appropriate for estimating other types

of ecological effects; however, for calculating the probability of extinction or decline of a listed species, demographic population models are the most practical and relevant tools available.

Using a population model requires three inputs. Two of the inputs are the outputs of the exposure and effects models described previously. Effects models describe the change in population-model parameters (survival and reproduction) as a function of pesticide concentration, and exposure models provide estimates of pesticide concentration over time and space. The third input is demographic and life-history information, such as age at first reproduction, age-specific (or stage-specific) survival and fecundity rates over time and space in natural populations, and mechanisms and magnitude of density-dependent processes.

There is a large variety of population models, from deterministic, exponential models of a single population to stochastic, age-structured or stage-structured, spatially explicit metapopulation models with complex forms of density dependence (see introductions and reviews in Burgman et al. 1993; Akçakaya et al. 1999, 2008; Quinn and Deriso 1999; Caswell 2001; Morris and Doak 2002; Pastorok et al. 2002 for topics covered in the sections that follow). The appropriate models for purposes of pesticide-effects modeling are complex, species-specific models that incorporate all the relevant demographic parameters and spatial structure required to predict extinction risk. Some species, such as North American Pacific and Atlantic salmon, have been carefully studied and probably have sufficient data to assign values to parameters in such models. However, many listed species have been studied in only a cursory manner, and modelers have only enough information to characterize the life history of a group of species and are only able to use simple, generic, deterministic models that predict λ , the finite rate of increase in the population. The committee concludes that in the absence of detailed demographic information, it is appropriate to use such models to characterize the baseline condition of a listed species, provided that the analyst incorporates estimates of uncertainty—for example, by using reasonable “high” and “low” demographic inputs—to bound the range of probable λ s and includes a discussion in the final risk assessment about the magnitude of the uncertainty resulting from this lack of knowledge.

The sections that follow discuss important issues related to various components of population models that are especially relevant to assessing the risks posed by pesticide exposure.

Temporal Scale

The temporal scale of an assessment has two components: the time step of the model and the time horizon (duration) of the assessment. For most species in temperate ecosystems with generation times of 1 year or longer, an annual time step is appropriate. Except for the simplest models, whose main result consists of asymptotic measures of population performance (such as λ), models that estimate population viability require specification of a time horizon. There

is a tradeoff between relatively short time horizons, which allow more reliable projections but might not be relevant for the conservation of the species (because the goal is long-term existence of the species), and relatively long time horizons, which are more relevant but result in more uncertain projections of population viability. Even if the effect at the individual level occurs for only a few years, population-level effects might be observed longer because of changes in the age structure of the population. To account for such transitory effects, an assessment can use a time horizon of several generations of the species or the period during which a pesticide is expected to affect the population, whichever is longer.

Spatial Scale

The spatial scale of an assessment has two components: resolution and extent. For most population models, the spatial resolution should coincide with the typical sizes of the areas (or ranges of sizes) occupied by populations or subpopulations of the species. That might require a translation of the results of the exposure model to reduce the spatial resolution to a level that is appropriate for the species. In other words, the results of exposure modeling at very fine resolution (for example, 30-m grid cells for a species with a 1-ha home range and populations occupying areas of several square kilometers) can be translated into effects at the population level by calculating an overall reduction in survival and reproduction in each population on the basis of the average EEC to which the population will be exposed. The average EEC would be estimated with errors by the exposure model, and the errors would be incorporated by using joint probability distributions (see Chapter 5).

Ideally, the spatial extent of the models would include all areas in which a modeled species is exposed to the pesticide being evaluated. Both the spatial distribution of the species and the distribution of pesticide in the landscape might be heterogeneous. As a result, different populations of the species might be exposed to different concentrations of the pesticide, and even individual organisms in a population might have different exposures. In some cases, spatial variability of exposure can lead to source-sink dynamics in a metapopulation (Palmqvist and Forbes 2008).¹ That is, populations that are exposed to the pesticide might become sink populations² and thus deplete the populations that are not exposed; conversely, exposed populations might remain extant despite exposure because of dispersal from the unexposed populations in the same metapopulation (Spromberg and Johnson 2008). Accordingly, if there is dispersal between populations, exposure of one population can cause a reduction in an-

¹A metapopulation is a set of populations of the same species in the same general geographic area that might exchange individual organisms through dispersal.

²A sink population has more deaths than births and remains extant only because there are more immigrants than emigrants.

other, unexposed population. Depending on the spatial separation of the areas, separate assessments can be performed for each area or a single assessment can be performed with a metapopulation model that represents each area as one or more populations.

The spatial variability of exposure would be estimated on the basis of spatially explicit projections of the exposure models, and the spatial variability in the species distribution would be based on the projections of a species-distribution model (an ecological-niche model or habitat-suitability model) that might be based on geospatial data (see the section "Characterization and Delineation of Habitat" in Chapter 3). The committee concludes that in the absence of spatial data, it is appropriate to use generic, single-population models with no spatial structure that include average exposure and environmental conditions expected in the exposed area of the species' range and to incorporate errors estimated with exposure modeling.

Temporal Variability

Variability (or stochasticity) refers to parameters of a population model that vary randomly, such as survival rates or fecundities in different age classes. Temporal variability means that models cannot predict the population size in the future precisely. Instead, they can project statistical distributions of future population sizes. The distributions are often used to calculate risks, such as risk of species extinction, risk of population extirpation, or risk of population decline to a predetermined level. Incorporating temporal variability results in a more realistic model that has more relevant end points, such as extinction risk. The committee concludes that population models that incorporate temporal variability and focus on probabilistic results are needed for assessing risks at the population level and that deterministic models are insufficient for this task. However, in the absence of such information, deterministic models with such end points as λ (the finite rate of increase) can be used as the initial step of risk assessment. In such cases, every effort should be made to obtain the data necessary to estimate temporal variability, and the uncertainties in the end points reported should be clearly described in the assessment with the recognition that a deterministic baseline model might bias the assessment. Notwithstanding the use of a deterministic baseline model, uncertainties in the exposure analysis and the dose-response analysis should be incorporated into a risk assessment, for example, by using joint probability distributions (see Chapter 5).

Density Dependence

Density dependence (most commonly, the reduction in fecundity and survival that occurs as population size increases and that results from competition for food, breeding habitat, or other critical resources) is an important aspect of the dynamics of many populations and their responses to toxicants (Forbes et al.

2001, 2003). In the absence of data on effects of density on population growth and for screening-level assessments, it is reasonable to use density-independent models. Such models often use population growth rate as the main result, although if the models are stochastic, they can also be used to estimate population viability (the probability of population decline or extinction over a specified period). Although density-independent models make a number of assumptions and leave out important aspects of population dynamics, their results are more relevant for assessing pesticide effects on species than the results of models that assess pesticide effects only on individual organisms.

If there is evidence that survival or reproduction changes as a function of population density, it is important to incorporate density dependence into a model. That a species is rare or has been in decline does not necessarily mean that its dynamics are not density-dependent. For example, if the species has been declining because of habitat loss, its dynamics are probably density-dependent. In addition, species that have declined to very low abundances might be subject to depensation or inverse density dependence, which is the reduction in survival or fecundity that occurs at low density and accelerates the species' decline and which is commonly referred to as Allee effects (Courchamp et al. 2008).

Incorporating density dependence into a model of a population whose vital rates (survival or fecundity) might be affected by pesticide exposure presents challenges (Moe 2007). For example, the pesticide exposure might reduce the growth rate of the population by the same amount regardless of population size. Those conditions would make the density-dependence functions of baseline and effects models (population models with and without pesticide exposure) have the same shape (Figure 4-1A). In other cases, the pesticide effects on the growth rate of the population might be stronger in large populations (Figure 4-1B) and result in more-than-additive (synergistic) effects, or the pesticide effects might be stronger in small populations (Figure 4-1C) and result in less-than-additive (antagonistic) effects (see, for example, Forbes et al. 2001; Moe 2007). Thus, pesticide exposure might reduce the carrying capacity (or equilibrium population size) directly (by reducing survival and fecundity at all densities) or indirectly (by, for example, reducing abundance of species on which the species of interest preys). Whether the effect will be additive, synergistic, or antagonistic depends on several factors, including which life-history stages are affected by toxicity and density dependence (Forbes et al. 2001). The committee concludes that it is not accurate to assume that mortality due to pesticide exposure will be compensated for by density dependence; it is likely that such exposure will decrease the growth rate of a population at all densities and generally depress the population growth-density curve as depicted in Figure 4-1.

MIXTURES

Effects analysis requires knowledge or judgment of the adverse effects associated with individual chemicals or chemical combinations at concentrations

predicted to occur in the exposure environment. The toxicity of a chemical mixture probably will not be known, and it is not feasible to measure the toxicity of all pesticide formulations, tank mixtures, and environmental mixtures. Therefore, combined effects must be predicted on the basis of models that reflect known principles of the combined toxic action of chemicals (El-Masri et al. 1997). This section discusses the state of the science of mixture toxicity, raises practical issues associated with mixture assessments, and provides a case study of the application of information in the context of assessing risks to listed species posed by pesticides.

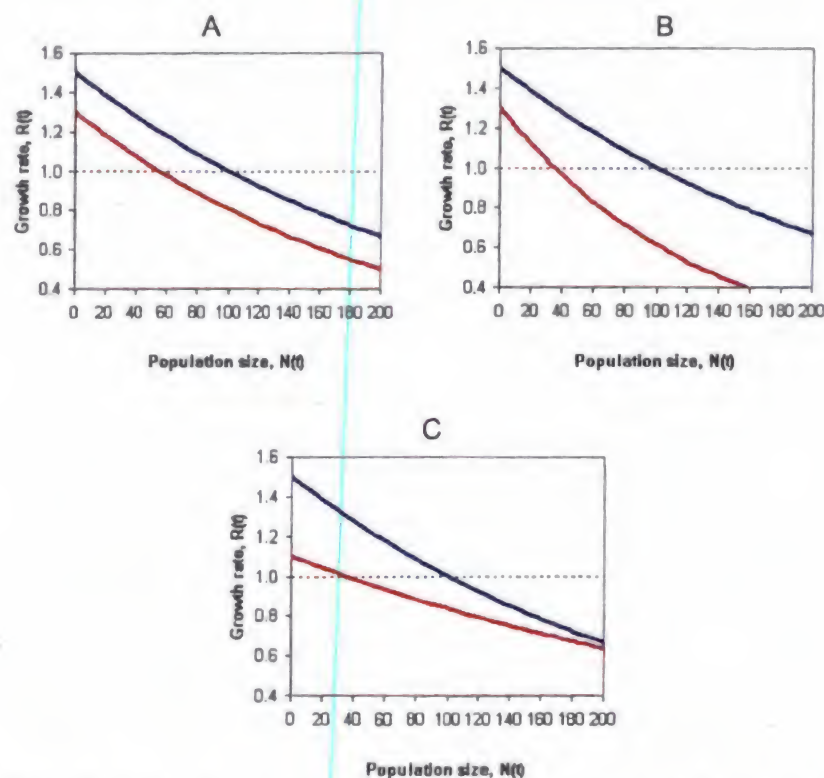


FIGURE 4-1 The effect of pesticide exposure on a density-dependence function. In all three graphs, the top curve shows the baseline model, and the bottom curve shows the effect model. Each curve shows the effect of density on population growth rate. Pesticide effects might decrease population growth equally at all densities (A), more at higher densities (B), or more at lower densities (C). Source: RAMAS 2011[®]. Reprinted with permission; copyright 2011, RAMAS[®]. RAMAS[®] is a registered trademark of Applied Biomathematics. See also Forbes et al. (2001) and Moe (2007).

Additivity and Interactions

The term *additivity* is used to designate forms of joint action in which the response to a mixture can be modeled on the basis of the expected responses to the mixture components in the absence of any toxic interactions. Two forms of additivity—concentration addition and response addition—are generally considered.³ Concentration addition assumes that the components of the mixture act by the same mechanism⁴ and that the components differ from each other only in their potency. Response addition assumes that the response to the mixture can be predicted on the basis of the expected responses to the individual components of the mixture. Toxic interactions are cases in which the joint toxic action of mixture constituents cannot be adequately described on the basis of additivity alone. Interactions are generally classified as synergistic (greater than additive) or antagonistic (less than additive). The frequency with which pesticide mixtures are found in surface waters is often cited as rationale for exploring the toxicity of pesticide mixtures (Scholz et al. 2006; Belden et al. 2007a; Laetz et al. 2009).

Concentration Addition

The central mechanistic assumption of concentration addition is that chemicals act by the same mechanism and differ from each other only in relative potency, with potency defined as the ratio of equitoxic doses. If the concentration of Chemical 1 associated with a given response rate is twice that of Chemical 2, Chemical 1 has half the potency of Chemical 2. Thus, relative potency can be used to convert an effective concentration of one chemical to a toxicologically equivalent concentration of another chemical.

Implicit in the application of concentration addition is the assumption that the slopes of the concentration-response curves for all mixture components are identical. The assumption of equal slopes follows directly from the assumption of functionally identical mechanisms of action. The slope of the concentration-response function is essentially a measure of the variability of individual tolerances in a population. Under the assumption that all chemicals in a mixture have the same mechanism of action, it follows that the distribution of individual tolerances and hence the shapes of the concentration-response curves will be the

³Concentration addition is also referred to in the literature as dose addition, simple similar action, or similar joint action. Response addition is also referred to in the literature as independent joint action or dissimilar joint action (see, for example, Bliss 1939; Finney 1971; EPA 2000). For consistency and simplicity, only the terms *concentration addition* and *response addition* are used in this discussion; it is recognized that *dose addition* is preferable to *concentration addition* when exposures are expressed as doses.

⁴*Mechanism* is defined in this context as the molecular interaction between a pesticide active ingredient and a biological target (for example, an enzyme or ion channel) that is responsible for the response being measured.

same for each chemical; hence, the slopes of the concentration-response functions of all the chemicals will be identical.

In practice, the slopes of the concentration-response functions will seldom be identical even for chemicals that have the same mechanism of action. Similarly, because of random variability, repeated bioassays of the same chemical on the same species by the same investigators will seldom have identical slopes. In such cases, methods are available for testing the significance of the differences between slopes and for constraining slopes to be parallel (Finney 1971). If the slopes of the concentration-response curves are identical (or can be constrained to be so without a significant lack of fit), the selection of the reference chemical for defining relative potency is incidental. That is, changing the reference chemical will change the relative potency values but will have no effect on the estimate of the concentration-response curve for the mixture.

In some cases, chemicals with the same mechanism of action at the receptor level can differ from each other in other ways (for example, differences in metabolic pathways) that can lead to differences in slopes in whole-animal studies. If the slopes of chemicals that act (or presumably act) similarly do differ, relative potency will vary with the magnitude of the response, and the application of concentration addition will be inappropriate.

Concentration addition is attractive because it is mathematically simple and is often viewed as a conservative assumption. As discussed below, concentration addition will typically predict a response rate that is equal to or higher than any form of response addition; it is conservative in this sense. Some groups have recommended concentration-addition as a general default method for mixture risk assessment, particularly for screening-level assessments (IPCS 2009; Kortenkamp et al. 2012). The EPA guidance for mixture risk assessment, however, recommends that concentration addition be applied only to groups of similarly acting chemicals (EPA 2000, p. 11). The committee concludes that the utility of concentration addition as a predictive and unbiased model for assessing joint action depends heavily on the underlying assumptions of concentration addition—similar mechanisms of action and parallel slopes. If those conditions are met, relative potency will be constant for all concentrations, so relative potency can be used to convert the concentration of one chemical into an equivalent concentration of another chemical. That conversion can be used to add concentrations correctly. If the underlying assumptions of concentration addition are violated, however, there is no reason to expect its application to be predictive. Application of concentration addition in those cases might lead to substantial errors that underestimate or overestimate the actual risk. Therefore, although the concentration-addition model has been demonstrated to predict the toxicity of pesticide active-ingredient mixtures more accurately when the pesticide active ingredients have the same mechanism of action (Belden et al. 2007a), caution should be exercised in using concentration-addition modeling as a default approach.

Response Addition

Response addition is a form of noninteractive joint action in which the response to a mixture is estimated on the basis of the responses (rather than the concentrations) that would be expected from the components of the mixture. Response addition does not assume that the components of a mixture act by the same or even a similar mechanism and does not assume anything about the slopes of the concentration-response curves. The slopes of the concentration-response curves for chemicals that have different mechanisms of action might or might not differ significantly. The only requirement is that the chemicals produce the same effect. In most practical applications of response addition, the end point is mortality; however, response addition can be applied to any quantal response. Response addition can take various forms, depending on assumptions about the correlation of tolerances in the population.

A review of the literature on pesticide-mixture toxicity revealed that the response-addition model provided somewhat more accurate predictions of toxicity than the concentration-addition model when the pesticide active ingredients had different mechanisms of action (Belden et al. 2007b). Response addition also has been shown to provide more accurate estimates of toxicity of mixtures that consist of dissimilarly acting pesticide and nonpesticide chemicals (Walter et al. 2002; Backhaus et al. 2004).

Synergy

Arguably, the greatest concern in evaluating hazards and risks to listed species posed by chemical mixtures that contain pesticides is whether constituents of the mixtures act to enhance the toxicity of the pesticide active ingredient. Indeed, pesticide synergists are often included in pesticide formulations (Jones 1998) and can enhance the toxicity of an active ingredient to nontarget organisms by a factor of 100 (Sahay and Agarwal 1997). The activity of some pesticide active ingredients also is substantially enhanced when they are administered in combination with other pesticides. Finally, chemicals to which coexposure occurs might increase the toxicity of a pesticide active ingredient by increasing its bioavailability or potency in the environment of the exposed organism.

Pesticide Formulation Synergists

Pesticide formulation synergists typically function by inhibiting cytochrome P450-mediated inactivation of the active ingredient (Hodgson and Levi 2001). They can enhance the effects of some pyrethroids, organophosphates, carbamates, and rotenone. Formulation synergists include bucarpolate, dietholate, iprobenfos, jiajizengxiaolin, MGK 264, octachlorodipropyl ether, piperonyl butoxide (PBO), piperonyl cyclonene, piprotal, propyl isome, sesamex, sesamol, sulfoxide, and zengxiaolan. PBO is among the most potent and widely

used formulation synergist (EPA 2005). Because formulation synergists are specifically used to increase the potency of pesticide active ingredients, they are most likely to produce the greatest enhancement of pesticide toxicity.

Toxicity evaluations that used the amphipod *Hyaella azteca* revealed that coexposure to PBO caused up to about a sevenfold increase in the toxicity of permethrin (Amweg et al. 2006). The synergistic potency of PBO increased as exposure concentration increased with a threshold concentration of 2.3 µg/L in water. The threshold concentration for synergy to occur stands in contrast to PBO surface-water concentrations, which are typically less than 80 ng/L even after direct application to surface water for mosquito abatement (Orlando et al. 2003, 2004; LeBlanc et al. 2004; Amweg et al. 2006). Given that *H. azteca* is considered sensitive to pyrethroids (Werner et al. 2010), that PBO is considered the most potent of formulation synergists, and that PBO concentrations in surface water after application tend to be below concentrations necessary to elicit synergism, there is a low probability that synergists associated with pesticide formulations enhance the toxicity of pesticide active ingredients. The greatest probability of synergistic effects might be when synergist-containing pesticide formulations are applied directly to aquatic systems or when there is direct contact between the formulation and a species.

Synergistic Interactions among Active Ingredients

As discussed in Chapter 3, pesticide active ingredients have the potential to coexist in tank mixtures or as environmental mixtures. In some cases, the toxicity of pesticide active-ingredient combinations has been shown to be greater than additive. The synergy has been exploited in recommended tank formulations to treat pests. With respect to nontarget species, the synergy has been recognized as a potential source of enhanced ecological threat. The following are examples of known synergistic interactions between pesticide active ingredients.

Organophosphates and Carbamates. Organophosphates and carbamates share a mechanism of action: inhibition of the enzyme acetylcholinesterase. Accordingly, the joint toxicity of organophosphates and carbamates should conform to a concentration-addition model. Indeed, the *in vitro* inhibition of acetylcholinesterase activity in salmon brains by combinations of organophosphates and carbamates showed that to be the case (Scholz et al. 2006). However, *in vivo* exposure of salmon to binary combinations of organophosphates, carbamates, or a combination of organophosphate and carbamate resulted in greater inhibition of brain acetylcholinesterase activity than would be predicted by concentration addition (Laetz et al. 2009). Serine esterases are important in the metabolic detoxification of organophosphates and carbamates (Cashman et al. 1996). Studies have shown that those esterases can be selectively inhibited by binding of one substrate, which results in increased toxicity of another because of its reduced detoxification (Murphy et al. 1959; Clement 1984).

Pyrethroids and Organophosphates. Studies in rodents (Ortiz et al. 1995) and insects (Martin et al. 2003) have shown that combinations of pyrethroids and organophosphates can synergize to produce greater than additive toxicity. Pyrethroids also are metabolized by serine esterases (Cashman et al. 1996), and it is reasonable to assume that various combinations of pyrethroids, organophosphates, and carbamates would have the potential to elicit greater than additive toxicity through the inhibition of serine esterases and perhaps other detoxification enzymes (Bielza et al. 2007).

Ergosterol Biosynthesis-Inhibiting Fungicides and Pyrethroids. Ergosterol biosynthesis-inhibiting (EBI) fungicides are potent inhibitors of some cytochrome P450 enzymes, and this inhibition is responsible for their mode of toxicity to fungi (Thompson 1996). Some EBI fungicides are imidazoles (for example, prochloraz and clotrimazole), triazoles (for example, propiconazole and tebuconazole), and morpholines (for example, fenpropimorph and aldimorph). Coexposure to some EBI fungicides and pyrethroids has been shown to result in greater than additive toxicity, presumably because of the inhibition of P450-mediated detoxification of the pyrethroids. The synergistic effect of EBI fungicides has been detected in a wide array of terrestrial and aquatic organisms (Norgaard and Cedergreen 2010; Bjergager et al. 2012) and reviewed in Cedergreen et al. (2006).

Synergy at High Laboratory Concentrations

Demonstrations of synergistic toxicity under controlled laboratory conditions often are performed at high chemical concentrations that are toxic even in the absence of synergy (see, for example, Anderson and Zhu 2004; Laetz et al. 2009). However, such synergy is of little use in identifying and quantifying synergy at low, environmentally relevant concentrations.

Many of the toxic mechanisms by which interactions might occur are saturable processes (such as rates of absorption, metabolism, and excretion), and many are governed by Michaelis-Menten or similar kinetics. In such processes, there are probably interaction thresholds—concentrations below which interactions are not likely to occur or, if they occur, will be minimal and probably not detectable (Figure 4-2). Toxic interaction thresholds have been described in terrestrial mammals (Dobrev et al. 2001; Yang and Dennison 2007; El-Masri 2010) and in aquatic organisms (Mu and LeBlanc 2004; Rider and LeBlanc 2005). Although the assessment of interaction thresholds is evolving, the current view, informed by empirical data, is that they are in the range of toxicity thresholds of the individual components of the mixtures (Yang and Dennison 2007). Similar observations were made much earlier and before the formal discussion of interaction thresholds (see, for example, Feron et al. 1995). Interaction thresholds make sense in the context of the underlying kinetics and might be useful in assessing whether concerns about potential toxic interactions are important in exposures to specific mixtures.

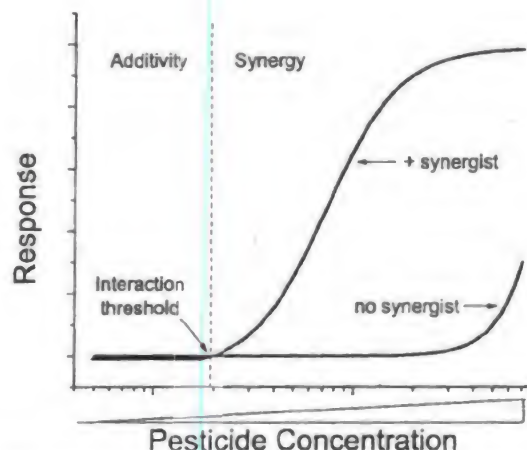


FIGURE 4-2 Concentration-response curve of a chemical in the presence and absence of a synergist. Toxicity of the chemicals is consistent with additivity below the interaction threshold and with synergy above the interaction threshold.

The existence of interaction thresholds does not necessarily reduce the probability of additive responses to mixtures of chemicals in which each chemical is below its own toxic threshold. In such cases, an additivity model might suggest the potential for a toxic response. The concept of interaction thresholds simply indicates that the probability of toxic interactions (as opposed to some form of additive joint action) is reduced if the total exposure does not exceed a threshold based on an assumption of additivity. A difficulty in the application of the concept of interaction thresholds is quantification of the threshold, which is difficult in the risk assessment of single chemicals and mixtures.

Uncertainty Factor to Account for Synergism

A specific charge to the committee was to "consider the selection and use of uncertainty factors to account for the lack of data on...synergy [and] additivity." The committee concludes that there is no scientific basis for applying a generic uncertainty factor under the presumption of a synergistic interaction. Doing so would introduce a bias into the risk assessment.

As an alternative to generic uncertainty factors, EPA's supplemental guidance for mixture risk assessment outlines a weight-of-evidence approach for incorporating quantitative consideration of interactions by using numerical binary weight-of-evidence scores that are based largely on qualitative information on potential interactions and any information on the magnitude of interactions of mixture components (EPA 2000, Section 4.3.1.1, pp. 90-103). That method was developed in the context of human-health risk assessment, and no examples of

its application to ecological risk assessment could be found. Furthermore, no studies or analyses that address the accuracy of the method in predicting responses to mixtures could be found.

Antagonism

Antagonism occurs when components of a mixture interact in a manner that results in toxicity that is less than would be predicted under an assumption of additivity. Antagonistic interactions that are most likely to affect pesticide toxicity occur when two components of a mixture are competing for the same target site of toxicity and the less toxic component competitively displaces the more toxic component or when a component of the mixture inhibits the metabolic conversion of a pesticide to a more toxic derivative. The former situation has been well described with binary combinations of pesticide active ingredients that share a mechanism of action. For example, exposure of the Asian catfish *Mystus vittatus* to the acetylcholinesterase inhibitors dichlorvos and thiotox or dichlorvos and carbofuran resulted in less toxicity than would be predicted on the basis of additivity (Verma et al. 1980). In both cases, exposure to the less toxic component at the maximum tolerated concentration reduced the toxicity of the more toxic constituent, presumably because of competitive displacement of the more toxic component from the target enzyme. Similar antagonistic effects have been observed with pairs of pyrethroid insecticides (Schleier and Peterson 2012).

Although PBO is typically used as a pesticide synergist by inhibiting cytochrome P450 activity, it and other cytochrome P450 inhibitors can decrease the toxicity of pesticides that are enzymatically converted to more toxic oxidative metabolites. For example, malathion and parathion are metabolically converted to their more toxic oxon derivatives by the actions of cytochrome P450s. Exposure of daphnids to either insecticide and PBO significantly reduced toxicity of the insecticides (Rider and LeBlanc 2005). Similar antagonism was observed with PBO and chlorpyrifos, which also is metabolically converted to the more toxic oxon derivative (Ankley and Collyard 1995; El-Merhibi et al. 2004).

The committee emphasizes that for a mixture component to antagonize (reduce) the toxicity of a pesticide active ingredient, the pesticide active ingredient must be present at a concentration that actually elicits toxicity. Given that circumstance, the committee concludes that ecological risk assessment should focus on the pesticide active ingredient alone and avoid the added uncertainties associated with estimating the reduction in risk due to the presence of an antagonist.

Complex Mixtures

Many environmental mixtures are highly complex, that is, contain a large number of components. That can complicate the exposure and effects analyses of the mixtures. As discussed at some length in EPA's supplemental guidance

on mixture risk assessment (EPA 2000), confidence in the application of component-based methods diminishes as the number of components of a mixture increases. For some highly complex mixtures, such as petroleum distillates and surfactants, component-based methods might be impossible because the components are not well characterized and toxicity data on them are lacking.

For complex mixtures, the preferred assessment method is to use data on the whole mixture, termed the *mixture of concern*. The toxicity of the mixture is assessed with a bioassay. A problem with the mixture-of-concern approach, however, is that the composition of many complex mixtures is variable. Often, toxicity data are not available on the mixture of concern but are available on similar mixtures. Addressing those types of situations involves an assessment of *sufficient similarity*, that is, determining which, if any, of the mixtures on which data are available can be used to assess the toxicity of the mixture of concern reliably. EPA (2000, p. 38) offers only brief and general guidance on assessing sufficient similarity:

In determining whether a mixture is sufficiently similar, consideration should be given to any available information on the components that differ or are contained in markedly different proportions from the mixture of concern. In addition, if information exists on differences in environmental fate, uptake and pharmacokinetics, bioavailability, or toxicological effects for either of these mixtures or their components, it should be considered in deciding on a risk assessment approach.

EPA (2000) also notes that the *comparative-potency method* might be useful in assessing toxicity of complex mixtures. Essentially, that method involves using toxicity data on complex mixtures for which two toxicity end points—for example, an LC_{50} and a reproductive no-observed-effect concentration (NOEC)—are known to estimate a toxicity value (say, a reproductive NOEC) for a mixture for which only the other end point (an LC_{50}) is known.

Simply because a mixture is complex does not indicate that the joint action of the mixture is complex. It is highly relevant to examine the frequency at which environmentally relevant chemical mixtures elicit cumulative toxicity. Olmstead and LeBlanc (2005a) evaluated the toxicity of a mixture of nine chemicals, including pesticides, at the median concentration in US surface waters as measured by Kolpin et al. (2002) and dilutions and fortifications thereof. The mixture elicited concentration-dependent toxicity at exposure concentrations between the median and 10 times the median concentrations of the chemicals, and the investigators were able to predict the toxicity of the mixture accurately with a model that combined concentration addition and response addition. However, further analyses revealed that the toxicity of the mixture could be explained largely by a single constituent, chlorpyrifos. The experiment was repeated without chlorpyrifos in the mixture. Toxicity was not eliminated by the removal of chlorpyrifos; rather, the remaining chemical mixture elicited toxicity at a higher concentration. Again, analyses of the responses to the individual

chemicals in the mixtures revealed that toxicity of the new chemical mixture was due to the actions of a single constituent in the mixture, diazinon. Thus, the chemical mixtures, at environmentally relevant constituent ratios, produced toxicity, but toxicity could be attributed primarily to a single constituent.

Adam et al. (2009) evaluated the aggregate toxicity to the amphipod *Gammarus pulex* of four pesticides—propiconazole, tebuconazole, 3-iodo-2-propinyl butyl carbamate, and cypermethrin—at concentration ratios typically found in commercial formulations. Toxicity of the mixture could be explained by the concentration of cypermethrin. Studies of environmental samples that contain chemical mixtures have typically shown that toxicity of the mixture can be attributed to one or a few constituents (Amweg et al. 2006; Belden et al. 2007a).

Although mixtures of pesticides and other chemicals clearly exist in the environment, the presence of a mixture does not necessarily imply toxicity. Furthermore, on the basis of mixture modeling theory discussed above, the presence of dissimilarly acting chemicals, each present at a concentration that elicits no toxicity, would not be predicted to elicit toxicity in a mixture in the absence of synergy. The presence of chemicals that have the same mechanism of action, each at a concentration that elicits no toxicity, would be predicted to elicit toxicity only if the combined, potency-normalized concentrations of the chemicals exceed the threshold concentration for a response.

Practical Issues in Assessing Effects of Pesticide Mixtures

Assessment of the effects of pesticide mixtures is associated with many practical aspects. This section first describes the positions taken and approaches used by EPA and the Services, then discusses various issues associated with pesticide formulations, and finally provides a perspective on the magnitude of interactions.

Agency Positions and Approaches

Approaches to addressing risks associated with exposures to mixtures are clearly a major source of disagreement between EPA and the Services, although the discord is not based on any fundamental disagreement about methods. The BiOps prepared by NMFS (2008, 2009, 2010, 2011) suggest that general guidelines used by EPA have been adopted by NMFS inasmuch as they reference EPA methods for ecological risk assessment (EPA 1998a, 2004). In specific and quantitative considerations of mixture exposures (for example, NMFS 2010, p. 465ff), the Services adopt concentration addition for mixtures of similarly acting pesticides, and this approach is consistent with the methods recommended by EPA (EPA 1986, 1989, 1998a, 2000, 2002).

Although EPA and the Services appear to accept the same basic methods in mixture risk assessment, their implementations of the methods differ substan-

tially. Each BiOp developed by NMFS expresses substantial concern for mixture exposures and the potential for synergistic effects. As discussed further below, similar concerns are also expressed by FWS. Although EPA guidelines (EPA 1998a, 2004) certainly recognize and appreciate the potential importance of exposure to mixtures, ecological risk assessments prepared by EPA focus on single active ingredients in the generic risk assessments (EPA 2004). The Services, in contrast, note a need to address exposures to all active ingredients *and* inerts that might affect populations of species (for example, FWS 2009).

Although diametrically opposed, the positions of the Services and EPA both have merit. EPA may elect to look at only single agents in most of its risk assessments, but agency-wide guidelines for mixture risk assessment, particularly EPA's *Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures* (EPA 2000), provide quantitative approaches for incorporating any available information on potential chemical interactions into a risk assessment. The approaches, however, are extremely labor-intensive, are accompanied by substantial uncertainties that are not readily quantified, and are best suited to site-specific analyses in which exposures to specific chemicals can be estimated with confidence. Thus, EPA takes the position that practical and unavoidable limitations in resources and data preclude a detailed quantitative assessment of chemical interactions, and the Services take the position that a quantitative assessment of interactions should be done. The committee concludes that quantitative assessment of chemical joint action is warranted if adequate data are available on the exposures to and toxicities of the chemicals. Approaches for such analyses are detailed further in the final section of this chapter, "Conclusions and Recommendations."

Formulation Toxicity

Several practical issues arise in the determination and use of data on pesticide formulations. There is the issue of availability of toxicity data on the inerts and the formulations themselves. There are also issues of the applicability of formulation data, particularly in considering long-term or chronic effects, and the applicability of formulation data that are extrapolated from other formulations. Those issues and others are discussed below.

Toxicity Data on Inerts

As discussed by Levine (1996), the original testing requirements for inerts in pesticide formulations were developed by the Food and Drug Administration, and these requirements were less rigorous than the testing requirements for the pesticides (that is, the active ingredients). In 2006, the EPA Inert Ingredient Assessment Branch completed a series of inert-ingredient tolerance-reassessment decision documents; however, documents covering all approved inerts do not appear to be available (EPA 2012b). One explanation is that tolerances are de-

veloped only for chemicals that are approved for use on food crops. List 1 inerts (toxic inerts) cannot be used on food crops and therefore do not have tolerance-reassessment documents. EPA has prepared guidance documents for companies involved in the development of new food-use inerts (EPA 20120c), new non-food-use inerts (EPA 2012d), and low-risk polymer inerts (EPA 2012e); additional guidance is provided in EPA's Pesticide Registration Manual (EPA 2012f). Although the documents do not contain an explicit list of required tests, they suggest that EPA could require the same types of tests as are required for active ingredients. With the exception of the guidance document on low-risk polymers, all the inerts guidance documents refer to the Office of Prevention, Pesticides, and Toxic Substances Harmonized Test Guidelines, which are used in the registration of pesticide active ingredients (EPA 2013). The committee found neither a specific list nor examples of the tests required for a new inert under EPA's guidance documents for developing new pesticide inerts.

Related to the availability of toxicity data and testing requirements for pesticide inerts is the determination of whether additional data are needed on them. EPA noted that it will often rely on acute toxicity studies of formulations in mammals to determine whether acute toxicity studies of formulations should be required in fish and invertebrate species (E. Odenkirchen, EPA, personal commun., April 4, 2012). Specifically, the agency referred to a series of standard studies often referred to collectively as the mammalian six-pack: acute oral toxicity (EPA 1998b), acute dermal toxicity (EPA 1996), acute inhalation toxicity (EPA 1998c), acute eye irritation (EPA 1998d), acute dermal irritation (EPA 1998e), and skin sensitization (EPA 2003). The extent to which those acute studies in mammals will be reliable in assessing the potential of inerts to enhance toxicity of pesticide active ingredients to fish and aquatic invertebrates is not clear. The committee identified no explicit analyses that support the use of mammalian six-pack studies of active ingredients and formulations to assess the potential of inerts to enhance toxicity to fish and aquatic invertebrates.

Toxicity Data on Formulations

Pesticide formulations are not tested as extensively as active ingredients. However, if data are available on both an active ingredient and a formulation, the contribution of inerts to the toxicity of the formulation can be at least crudely assessed. All pesticide formulations must identify the percentages of their active ingredients. If $\pi_{a,i}$ is the proportion of an active ingredient in a formulation and ζ_F is the toxicity value for the formulation, such as the LC_{50} , the toxicity value of the active ingredient ($\zeta_{a,i}$) is the product of those two terms. $\zeta_{a,i}$ can then be compared with experimentally determined toxicity values of the active ingredient alone. If, for example, the LC_{50} of the active ingredient as part of the formulation is substantially lower than the LC_{50} of the active ingredient alone, it suggests that some components of the formulation might be contributing substantially to the toxicity of the formulation. Conversely, if the LC_{50} of the

active ingredient as part of the formulation is substantially higher than the measured LC_{50} of the active ingredient alone, it suggests that some components of the formulation might be reducing the toxicity of the active ingredient. That type of comparison often yields the only type of quantitative information that can be used to assess the toxicological importance of inerts in a formulated product.

Chronic toxicity studies are not generally conducted on pesticide formulations and are not available on most inerts. In cases in which a chronic toxicity value is available for an active ingredient ($Ch_{a.i.}$) and acute toxicity values are available for the active ingredient alone ($Ac_{a.i.}$) and the active ingredient as part of the formulation (Ac_{Form}), a chronic toxicity value for the formulation (Ch_{Form}) could be estimated by using the following formula:

$$Ch_{Form} = \frac{Ac_{Form}}{Ac_{a.i.}} Ch_{a.i.} \quad (\text{Eq. 1})$$

where all toxicity values are expressed in units of active ingredient.

The above approach raises important issues. A major assumption is that acute toxic potency and chronic toxic potency will be the same or at least closely related. Acute toxicity end points, such as mortality, will often bear little relationship to chronic end points, such as growth and reproductive capacity, and there will be little or no basis for assuming that the underlying mechanisms of action in producing acute and chronic effects are comparable. The approach becomes more palatable when the same mechanism-based end point is used for acute and chronic toxicity evaluations. For example, cholinesterase inhibition might be considered for assessing responses to acute and chronic exposures to an organophosphate or carbamate insecticide. Again, the major impediment to the use of the approach is the general lack of mechanism-based data on effects after chronic exposure.

Environmental Partitioning and Applicability of Formulation Studies

A major reservation in the use of formulation studies concerns environmental transport. Unless an active ingredient and inerts in a formulation have similar chemical-fate and environmental-fate properties—this is seldom the case—the active ingredient and the other components of the formulation will partition at different rates in various environmental compartments (see Chapter 3). If the partitioning is substantial, as is often the case, there is little rationale for asserting that differences in acute toxic potency will have any relationship to differences in effects of chronic exposures, a relationship that is assumed in the approach described above.

Considerations of environmental partitioning also affect the usefulness of chronic studies of formulated products. Although longer-term studies can be conducted on pesticide formulations, such studies typically involve designs in

which partitioning processes do not occur. The studies can provide useful information on the long-term effects of a formulation as it is applied, but these exposures probably have little relevance to exposures that occur in the environment as environmental partitioning occurs.

In some cases—for example, the Roundup formulations of glyphosate (EPA 2008)—detailed information is available on the toxicity of an active ingredient, the toxicity of specific inerts, and the toxicity of a formulation. In such cases, more detailed assessments can be conducted on the basis of analyses of toxic interactions or available data on the mixture of concern.

Data-Bridging

Another problem that arises in using formulation studies to assess the toxicity of inerts in pesticide formulations concerns “data-bridging.” Although EPA generally requires at least acute toxicity data on pesticide formulations, it will often allow toxicity studies on one formulation to support the registration of another. That general approach is sometimes referred to as bridging registration (EPA 2012f). Data-bridging is used in the United States (EPA 2002, 2012f) and member nations of the Organisation for Economic Co-operation and Development (OECD 2001). Although data-bridging is motivated by economic factors (reducing the costs associated with pesticide registration) and ethical factors (reducing the number of animals that must be used in toxicity studies), the process of data-bridging must be supported by similarities between the two formulations to be scientifically credible.

The committee concurs that data-bridging is sensible if two formulations are identical (the same formulation marketed under different names). If two formulations are substantially different, however, formulation-specific data are required. Recently, EPA (2012g) released relatively detailed guidance for waiving mammalian acute toxicity studies. Although the document is titled *Guidance for Waiving or Bridging of Mammalian Acute Toxicity Tests for Pesticides and Pesticide Products*, the main focus concerns the criteria for waiving acute toxicity studies rather than for bridging data among formulations. The OECD guidelines (OECD 2001, p. 89ff) articulate bridging principles that are generally consistent with EPA’s approach to assessing sufficient similarity. However, formulation-bridging is not transparent. In the absence of information, uncertainty can lead to assumptions that are not justified.

Foreign Formulations

Information is sometimes available on the toxicity of pesticide formulations used outside the United States. If comparable information is available on the US and foreign formulations, the information on the US formulation should take precedence because it will be the most applicable. If information is not available on the US formulation, the relevance and utility of the information on

the foreign formulation will be difficult to assess. For example, EPA's ecological risk assessment of glyphosate (EPA 2008) concludes that the probability that glyphosate will affect reproduction of mammals and birds is minimal, and similar conclusions have been drawn in several other risk assessments of glyphosate (WHO 1994; Giesy et al. 2000; Williams et al. 2000). One study in the South American literature, however, indicates that exposure to a South American formulation of Roundup, which contains glyphosate and proprietary surfactants, reduces testosterone concentrations in rats (Dallegrave et al. 2007). Similar reductions were observed in mallards after exposure to a South American formulation of Roundup (Oliveira et al. 2007). As part of the public comments on the registration review of glyphosate, it has been suggested that EPA use the data on the South American formulations to assess the risks to birds and mammals associated with exposures to US formulations (BeyondPesticides 2009); that is, the information on the foreign formulations should essentially be bridged to US formulations. Although pesticide manufacturers are required to disclose information on the composition of pesticide formulations registered in the United States to EPA, the requirement does not extend to pesticide formulations used only outside the United States. Therefore, EPA and the Services probably do not have access to information that would be useful in assessing the similarities or dissimilarities between US and foreign formulations. In the absence of that information, the merits of including data from studies of foreign formulations cannot be determined.

Magnitude of Interactions

EPA seldom addresses interactions quantitatively in ecological risk assessments of pesticides. In three BiOps, NMFS (2008, 2009, 2010) does address information on joint action and relies primarily on the publication by Laetz et al. (2009), which assayed acetylcholinesterase inhibition in Pacific salmon (*Oncorhynchus kisutch*) for all binary combinations of three organophosphates (diazinon, malathion, and chlorpyrifos) and two carbamates (carbaryl and carbofuran). The study by Laetz et al. (2009) notes interactions that range from additivity to synergism with an increasing prevalence of synergism as the exposures increased. The latter observation is consistent with the concept of interaction thresholds described above. The BiOps, however, do not attempt to use the information from Laetz et al. (2009) to adjust estimates of expected biological responses to mixtures quantitatively. NMFS (2009, p.266) noted that "we are unable to create a predictive model of synergistic toxicity as dose response relationships with multiple ratios of pesticides are not available and the mechanism remains to be determined." Other BiOps contain similar language and express concerns about mixtures.

EPA's agency-wide supplementary guidance for mixture risk assessment (EPA 2000) discusses methods for quantitatively addressing toxic interactions, but the methods are cumbersome to apply, and experiments that would be useful

in assessing the predictive value of the methods seem not to have been conducted. The guidance document, however, reviews studies of the acute toxicity of all possible binary combinations of more than 50 industrial chemicals in rats (Smyth et al. 1969) and notes that deviations from the assumption of additivity span a factor of about 5 (expected to observed ratios of LD₅₀ values of binary mixtures range from about 0.2 to 5). More recently, Boobis et al. (2011) searched publications on mammalian toxicology from 1990 to 2008 for studies reporting synergy at low sublethal doses. They discerned a maximum magnitude of synergy of about 3.5. The studies suggest that chemical interactions can modify toxicity, typically by less than a factor of 10. Exceptions do exist. PBO was shown to decrease the toxicity of malathion to daphnids (*Daphnia magna*) by as much as a factor of 100 (Rider and LeBlanc 2005), and the pesticide synergist *N*-octyl bicycloheptene dicarboximide increased the toxicity of deltamethrin to a snail (*Lymnaea acuminata*) by as much as a factor of 300 (Sahay and Agarwal 1997).

A Case Study: Assessing Pesticide-Containing Mixtures

Conventional approaches to assessing the risks posed by exposure to chemical mixtures first determine EECs of the mixture components and then estimate the hazard associated with those exposures. The approach is most appropriate for estimating whether the margin of safety for exposed listed species is sufficient. Table 4-1 provides a hypothetical dataset to exemplify how hazard from exposure to a pesticide in combination with other chemicals in the environment could be assessed by using established approaches discussed in this report. The listed species of concern in this exercise is sockeye salmon (*Oncorhynchus nerka*), and the pesticide of concern is cypermethrin, a pyrethroid. The cypermethrin is in a formulation that also contains the synergist PBO. The formulation will be added to a tank mixture that contains another pyrethroid insecticide, deltamethrin; a surfactant, Polysorbate-20; and a stabilizer, Epoxisoy. Contents of the tank mixture will be used for insect-pest control according to label specifications. And, several chemicals—nonylphenol, ethinyl estradiol, caffeine, acetaminophen, PBO, and cypermethrin—are known or predicted to be present in the exposure environment at measurable concentrations. Thus, the salmon might be exposed simultaneously to nine chemicals that originate from various sources. At issue is whether exposure to the chemical mixture poses a risk to the salmon.

Columns 2, 3, and 4 in Table 4-1 depict the sources of the chemicals and their concentrations in the different sources. Exposure of salmon to the mixture constituents can be estimated from those data. For example, cypermethrin is present in the formulation at a concentration of 0.05%. Once in the tank mixture, cypermethrin is diluted to a concentration of 250 mg/L (ppm), and the predicted concentration in the environment is 0.01 µg/L (ppb). The concentration of cypermethrin in the formulation can be derived from the label, the concentration in

the tank mixture is calculated on the basis of the dilution to which the formulation is subjected, and the environmental concentration would be determined from modeling using, for example, PRZM2/EXAMS II.

Column 5 of Table 4-1 presents the final environmental exposure chemical concentrations, which are the sums of the concentrations of the individual chemicals in Column 4 (environmental exposure concentration). Most of the values are the same as presented in the previous column unless the chemical appears twice. For example, cypermethrin was present in the formulation to be applied with a residual amount (0.005 ppb) already present in the environment; thus, the final concentration of cypermethrin in the exposure environment is the sum of the two concentrations. The exposure analysis concerning the mixture of chemicals present in the environment is arguably the most challenging aspect of the mixture risk assessment owing to the high degree of uncertainty about the identity of chemicals and their environmental concentrations. Column 6 of Table 4-1 identifies chemicals expected to elicit toxicity by the same mechanism of action: chemicals that act similarly are assigned the same letter. Thus, cypermethrin and deltamethrin are both expected to elicit toxicity through the disruption of axonal sodium channels and are both assigned the letter a. Nonylphenol and polysorbate 20 have the ability to mobilize the pesticide and are identified with the letter b. Nonylphenol and ethinyl estradiol elicit estrogenic activity and are therefore identified with the letter c.

It is necessary at this stage to identify the adverse response of the listed species that is deemed most relevant to the pesticide of concern. In this exercise, disruption of axonal sodium channels is assumed to be the mechanism of action, and immobilization and loss of equilibrium are identified as the relevant responses because these sublethal responses are considered indicative of impending lethality or reproductive impairment. The other eight chemicals are considered only in their potential capacity to modify that response to cypermethrin. Thus, reproductive impairment associated with the combined estrogenicity of nonylphenol and ethinyl estradiol would not be considered relevant to the assessment of cypermethrin and would not be integrated into the toxicity assessment. If one or more components of the environmental mixture were predicted to elicit toxicity independently of cypermethrin, risk assessments of those components might be warranted.

Column 7 (K values) of Table 4-1 identifies chemicals that have the potential to enhance the toxicity of cypermethrin and the similarly acting chemical deltamethrin in a nonadditive manner. That would include synergists, PBO in this exercise. The modifying effect of the synergist PBO on the response to cypermethrin and deltamethrin is defined by a coefficient of interaction (K) (Mu and LeBlanc 2004; Rider and LeBlanc 2005; TenBrook et al. 2010), which can be viewed as a special case of the coefficient of synergism (κ) as described by Finney (1942). K values are typically determined experimentally by assessing the effect of increasing concentrations of a synergist on a specific response to a pesticide—such as an estimate of the effective concentration at which 50% of

TABLE 4-1 Example Dataset Used to Assess Exposure to and Effects of Cypermethrin, in Mixture with Several Other Chemicals, on the Sockeye Salmon, *Oncorhynchus nerka*

1	2	3	4	5	6	7	8	9
Chemical	Formulation (%)	Tank (ppm)	Environment (ppb)	Final Exposure Concentration (ppb)	Similar-Acting ^a	K Values	EC ₅₀ (ppb)	Slope
Formulation ^b								
Cypermethrin	0.05	250	0.01	0.015	a		5.0	14
PBO	1.0	5,000	0.2	0.205		Cyper: 1.0 ^c Delta: 1.0 ^c	10,000	5.0
Tank								
Deltamethrin		100	0.004	0.004	a		3.1	15
Polysorbate 20		10,000	0.40	0.40	b		25,000	2.3
Epoxisoy		5,000	0.20	0.20			75,000	3.3
Environment								
Nonylphenol			0.001	0.001	b,c		1,500	5.7
Ethinyl estradiol			0.05	0.05	c		1,400	6.1
Caffeine			500	500			33,000	3.9
Acetaminophen			0.01	0.01			100	6.3
PBO			0.005					
Cypermethrin			0.005					

^aChemicals that act similarly are assigned the same letter.

^bFormulations can be evaluated for the potential contribution of inerts as described in the section "Formulation Toxicity."

^cK values of 1.0 were assigned to the synergist PBO because the environmental exposure concentration of PBO in this exercise was considered to be below the interaction threshold.

the population exhibits a defined response (an EC_{50})—in a surrogate species (Figure 4-3). Thus a K value of 2.0 would indicate that the corresponding concentration of synergist in the exposure environment would be expected to increase the toxicity of a pesticide by a factor of two (Figure 4-3). Alternatively, K values can be estimated on the basis of the available literature on the modifying effect of a synergist on the toxicity of a pesticide. K values also can be derived for factors that affect the environmental availability of a chemical (for example, enhanced mobility or dissolution because of a surfactant). However, those modifying effects would be more appropriately addressed when modeling environmental exposures.

Columns 8 (EC_{50}) and 9 (Slope) of Table 4-1 define the toxicity of each chemical with respect to the response of concern (immobilization or loss of equilibrium in this exercise). The concentration-response curve is used to define the EC_{50} and the slope (or power) of the relationship. Those values are required for later mixture modeling. Typically, the data are determined experimentally by using a surrogate species after an appropriate exposure duration. EC_{50} data are often available from the literature, and EC_{50} and slope values are required for FIFRA guideline studies.

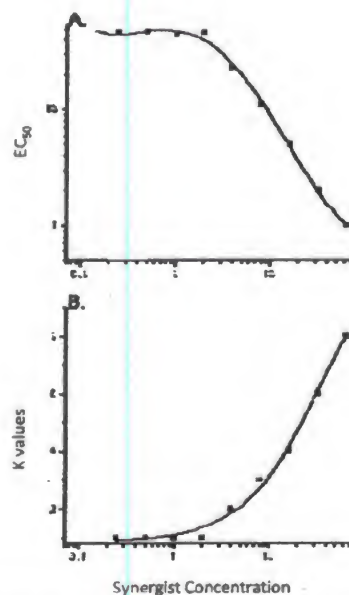


FIGURE 4-3 Example derivations used to determine K values. (A) Measured effect of the synergist on the EC_{50} of the chemical of interest. (B) K values at various concentrations of the synergist, calculated as the ratio of the EC_{50} of the targeted chemical in the absence of the synergist to the EC_{50} in the presence of a defined concentration of the synergist.

The response of the salmon to the toxicity of cypermethrin and the chemical mixture at the exposure site can be calculated from the data. First, the response to cypermethrin and deltamethrin at the exposure site is calculated with a concentration-addition model. Several concentration-addition model formats have been developed (Niederlehner et al. 1998; Safe 1998; Altenburger et al. 2000; Cleuvers 2003; Olmstead and LeBlanc 2005b) that are derivations of the original model presented by Finney (1942). Next, the responses (immobilization and loss of equilibrium) to each chemical, or groups of similarly acting chemicals, in the mixture are calculated with a response-addition model. The model originally described by Bliss (1939) remains the model of choice for calculating the joint action of dissimilarly acting chemicals (Backhaus et al. 2000; Walter et al. 2002; Olmstead and LeBlanc 2005b). Individual responses are then multiplied by appropriate K values to account for synergistic interactions. In this exercise, the K values of PBO are both 1.0; this indicates that the PBO concentration in the environment is not expected to modify the toxicity of cypermethrin or deltamethrin. Finally, the adjusted individual responses are summed to provide an estimate of the predicted response to the chemical mixture.

Data requirements and logistical considerations often temper efforts to assess the toxicity of chemical mixtures. Decisions on which chemicals in a mixture have the highest probability of toxic interaction with the pesticide active ingredient must be made and used to focus the assessment. Guidance for that decision-making is summarized in the section "Conclusions and Recommendations" of this chapter. Ultimately, some judgment must be made as to whether the possible adverse consequences associated with ignoring mixture effects outweigh the uncertainty associated with using nonempirical approaches to fill data gaps and to estimate the effects of mixture constituents on pesticide toxicity.

INTERSPECIES EXTRAPOLATIONS AND SURROGATE SPECIES

Different species often respond differently to chemical exposures because of differences in, for example, metabolic rates and pathways, the presence of functional genes, and different enzyme systems. Those differences can result in large differences in sensitivity; for example, adult guinea pigs (*Cavia porcellus*) are up to 5,000 times more sensitive to dioxins than are hamsters (*Mesocricetus auratus*) (Kociba and Schwetz 1982). Therefore, there is concern about how to extrapolate toxicity information from tested species to species of concern. Although the idea of finding a scientifically credible surrogate species might be appealing, the committee finds this approach difficult for two reasons.

First, it is not always straightforward to select a scientifically credible surrogate for a listed species. For example, rainbow trout are often used as surrogates for endangered Pacific salmon species because they are in the same genus, but they might respond differently to chemicals and other environmental stressors (Buhl and Hamilton 1991; EPA 2007). Moreover, there are seasonal differences in timing of breeding and larval development among species—generally,

trout in the spring and salmon in the fall (Quinn 2005)—and differences among species in sensitivity during development, juveniles being more sensitive than larval fish (Buhl and Hamilton 1991). Consequently, exposure at a given place and time will have different effects among species because of their inherent vulnerability and differences in timing of development (see Box 4-1). There are many other physiological and ecological differences among species that will also affect their vulnerability to stressors, such as temperature and disease, so the overall effect of exposure to contaminants at a given time of the year can vary considerably.

Second, not all species are amenable to the degree of domestication required to conduct laboratory experiments, and the use of some might lead to public objections if they are suggested for such studies, for example, dogs as wolf surrogates or cats as jaguar or ocelot surrogates. It is also hard to imagine an appropriate surrogate for many species, such as polar or grizzly bears. Therefore, a scientifically credible alternative approach is to define a range of sensitivities within which the sensitivity of a species of concern could reasonably be expected to occur or a range that could be used to make reasoned extrapolations from species that have been tested by using inferences based on other chemicals. Life histories would need to be considered. If different life histories lead two related species that have similar toxicological sensitivities to a chemical to occupy different locations at different times, their susceptibility to a chemical could be quite different.

Listed species are not inherently more sensitive to chemicals than species that are not listed (Sappington et al. 2001; Besser et al. 2005; Dwyer et al. 2005), so similar methods of cross-species extrapolations can be used for any ecological risk assessment. Those methods include interspecies correlation analyses or interspecies correlation estimation (ICE) (Dyer 2006; Raimondo et al. 2010) and species sensitivity distributions (SSDs) (Posthuma et al. 2001). ICE models use the initial toxicity estimate for one species to estimate toxicity values for other species. The toxicity values can then be used either directly (if the species whose values are predicted is the species of concern) or in the development of SSDs. Knowledge about the mechanism of action of a chemical and the physiological similarity between test species and species of concern can provide empirical evidence to use in interpreting the theoretical relationships derived with the ICE model. Dyer et al. (2006) showed that using estimated values in an SSD in addition to or instead of measured values results in identification of threshold concentrations within an order of magnitude of those derived from distributions based only on empirical data. If a small dataset is available, bootstrapping or a Monte Carlo analysis may also be used to generate a response distribution (Warren-Hicks and Hart 2010). Bayesian approaches, which use all the information underlying the concentration-response data and result in presentation of the entire range of values that could be encountered beyond those of the tested species, have also been used to generate the end-point values for use in an SSD (Moore et al. 2010).

An SSD is a statistical distribution of the various concentrations at which different species have the same response to a chemical (Posthuma et al. 2001). Figure 4-4 provides an example of an SSD. The simplest approach is to display the SSD as a cumulative distribution function in much the same way that inter-individual variability is displayed as an exposure-response function. An SSD can be based on any outcome—such as mortality, growth, or enzyme activity—for any group of species (such as all aquatic species, fishes, or plants) for any metric, such as EC_{50} , NOEC, or LC_{50} . Generally, a lognormal distribution is assumed, although Newman et al. (2000) point out that such an assumption is not always valid and that when sufficient data are available a data-specific distribution should be used. At the very least, the model's goodness of fit should be evaluated or acknowledged (Farrar et al. 2010). Furthermore, the data points used to generate the SSD have associated uncertainty that should be carried forward in generating the distribution. That uncertainty can be used to put confidence limits around the hazard concentration (HC) at the selected percentile and to determine the number of data points needed to define the HC with a desired amount of precision. Generally, the 5th percentile of the distribution is accepted as a matter of policy as the concentration that would maintain the viability of most species (HC_5), and preference is given to using the lower confidence limit of the HC_5 . The HC_5 s from SSDs of multiple chemicals for aquatic organisms—whether based on tested species or on extrapolations from ICE models—have been shown to be significantly lower than concentrations derived by using safety factors of 10 and 97% lower than the LC_{50} s of all endangered species (Raimondo et al. 2008).

A reasonable alternative to the use of SSD models is to use concentration-response models (or single-point estimates) available for each species to assign values to parameters in the population model with a Monte Carlo approach. For example, the percentage of the population that survives an estimated exposure can be randomly selected from all the species tested. At the exposure concentration of interest, survival might be 50% for a population of quail, 75% for a songbird, and 30% for a duck. One of those values would be randomly selected, and the population model would be run to determine the population-level end point (for example, lambda or risk of extinction or decline); that process would be repeated 1,000 times to generate a distribution of the population-level end points that reflects the range of possible survival rates of the nontested species at the estimated exposure concentrations. That approach assumes that the species of interest has an unknown survival rate that is encompassed by the range of survival rates of all other measured species. The latter species could be constrained to ones that are similar taxonomically (or physiologically) to the species of concern, or all species could be included to make the resulting analysis as robust as possible. All types of population-level end-point values (such as median, mean, and upper or lower bounds) are carried forward to the risk characterization. The process outlined here would be conducted simultaneously for reproduction.

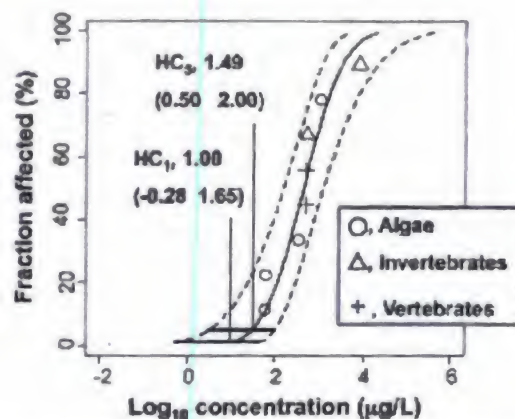


FIGURE 4-4 Species sensitivity distributions for 2,2'-dipyridyldisulfide derived by using a Bayesian statistical model. Source: Mochida et al. 2012. Reprinted with permission; copyright 2012, *Aquatic Toxicology*.

The committee concludes that the procedures outlined above, which result in a range of sensitivities, are good alternatives to the use of a single surrogate species. The use of a single surrogate species is often difficult to justify, but the use of a set of species would give a good idea of the range of possible organismal responses to a pesticide. As noted, life-history variations would need to be considered.

OTHER UNCERTAINTIES IN EFFECTS ANALYSIS

An effects analysis describes how a species of concern or a biological component of its habitat responds when exposed to a stressor, in this case a pesticide formulation, including the active ingredient and other constituent chemicals. It also includes an analysis of how the pesticide interacts with other environmental stressors, either increasing or decreasing the toxic response. However, all such estimates are uncertain, because of either measurement error or lack of knowledge. As stated in Chapter 2, the uncertainty should be clearly defined and propagated through the risk assessment. Currently, EPA and the Services do not quantitatively incorporate uncertainty in the effects analysis. Although they all report confidence intervals around most of the effects end points, they ultimately use only deterministic approaches (single point estimates of the magnitude of effect at a particular exposure concentration) or qualitative descriptions (particularly for behavioral and sublethal effects other than quantifiable reproduction responses). And they do not explain their selection of particular effects concentrations when selecting toxicity thresholds (for example, the choice of an EC₂₅ instead of an EC₁₀, or vice versa). Therefore, much quantitative information that

could explain the possible range of effects at single or multiple exposure concentrations is not used. General statements about “uncertainty” or “considerable uncertainty” are made, and these provide little or no guidance to a decision-maker because the terms are vague and open to multiple interpretations.

The committee recommends that all parties use quantitative uncertainty analyses whenever sufficient data are available. Selection of a particular approach depends on the amount of data available, the timeframe for conducting an assessment, and the preference of the risk assessors. Nearly all toxicity studies provide some information about concentration-response relationships, including measures of variability; and many measured environmental-response variables, such as productivity rates, also have time-dependent variability estimates. Therefore, quantified uncertainty estimates about effects values can be developed and used in the risk assessments. There are many well-documented methods for quantifying uncertainty in chemical toxicity assessments and in population models that are supported by user-friendly commercial software, including probability bounds, confidence intervals, Monte Carlo analysis, and Bayesian techniques (Spear 1997; Borsuk et al. 2004; Solomon et al. 2008; Link and Barker 2010; Warren-Hicks and Hart 2010; McLaughlin and Jain 2011). If quantitative effects data are insufficient for input into a quantified risk assessment or a quantitative uncertainty analysis, a qualitative statement about the risk potential and degree of uncertainty (such as low, medium, or high) can be used instead provided that they are accompanied by some bounding definitions (such as different by orders of magnitude). In cases in which some effects have quantifiable uncertainty and others do not, the committee recommends that the formal risk assessment focus on end points that are quantifiable and include quantitative measures of variability. The “others” should be described qualitatively and used as supplemental information after qualitative uncertainty categories or lines of evidence that might be useful are clearly defined.

CONCLUSIONS AND RECOMMENDATIONS

Sublethal, Indirect, and Cumulative Effects

- An adverse effect should be defined by the degree to which an organism’s survival or reproduction is affected; thus, assessing the effects of a pesticide on a listed species requires quantifying the effect of the pesticide on survival and reproduction of the species in the wild. Any effect that results in a change in survival or reproduction is relevant to the assessment, and any effect that does not change either outcome is irrelevant with respect to a quantitative assessment of population effects.
- To determine whether a pesticide is “likely to adversely affect” a listed species, a broad search should be conducted to identify information on sublethal effects of the pesticide and possible concentration-response relationships.

- To provide information to support a jeopardy determination, the Services should either (a) show how sublethal effects change survival or reproduction and incorporate such information into the population viability analysis or (b) state that such relationships are unknown but possible and include a qualitative discussion of uncertainty in the BiOp.
- When indirect effects can be quantified, they should be incorporated into the effects analysis.
- Population models provide an appropriate framework for incorporating baseline conditions and projected future cumulative effects into the assessment. Evaluation of those effects is within the purview of the Services and an appropriate part of the BiOp.

Effects Models

- Because the ESA is concerned with species or listed units within named species, the effects of pesticides must be expressed at the population level. Accordingly, population models that incorporate temporal variability and focus on probabilistic results are needed for assessing population risks. Although deterministic projection models are insufficient for that task, they can be used in the absence of information on temporal variability in the elements of the baseline model provided that the risk assessment recognizes the potential bias that might result from using them.
- Spatial structure and density dependence might have important effects on population dynamics and must be incorporated into population models when data are available. However, in the absence of such data, it is appropriate to use generic, single-population models that characterize the life history of a group of species to estimate the effects of a pesticide on a given species.
- The assumption that mortality due to pesticide exposure will always be compensated for by density dependence is not scientifically valid because such exposure will likely decrease the growth rate of the population at all densities and generally depress the population growth-density curve.
- For the purposes of population modeling, effects need to be estimated at a range of concentrations that includes all values that the population might reasonably encounter. Test results expressed only as threshold values or point estimates—such as the no-observed-adverse-effects level, the lowest observed-adverse-effects level, and the LC_{50} —do not provide enough information for a population-level risk assessment.

Mixtures

- A quantitative mixture risk assessment requires extensive data, including data on the identity, concentration, and toxicity of mixture components. Challenges in assessing risk to listed species from pesticide-containing mixtures

arise largely because of the lack of such data *and* the lack of understanding of the potential for interactions among mixture components.

- In the absence of such quantitative data, the possible contribution of specific mixture components to the toxicity of a pesticide active ingredient cannot be incorporated into a quantitative risk assessment. However, the risk assessor should describe the possible effects of mixture components on the risk estimate to the decision-maker.

- The committee emphasizes that the complexity of assessing the risk posed by chemical mixtures should not paralyze the process. The following guidelines provide a tool for helping to determine when and how to consider components other than the pesticide active ingredient in a risk assessment:

1. The toxicity of the pesticide active ingredient is central to the assessment. Other chemicals are relevant only if they modify the toxicity of the pesticide active ingredient or the susceptibility of the species of concern to the active ingredient.
2. The toxicity end point most relevant to the species of concern must be determined before initiation of the effects analysis.
3. Mixture components that do not elicit the relevant response in the species of concern do not need to be considered in the effects analysis. Mixture components that do elicit the relevant response need to be considered in the effects analysis.
4. In the absence of any data that would support the hypothesis of a synergistic interaction between the pesticide active ingredient and other mixture components, the effects analysis should proceed on the assumption that the components have additive effects.
5. For chemicals that have common mechanisms of action and parallel slopes in the concentration-response curves, concentration addition is a reasonable approach for modeling additive effects. However, caution should be exercised in using concentration-addition modeling as a default approach when no mechanistic data or concentration-response data are available.
6. For chemicals that have different mechanisms of action, response addition (with a zero correlation of individual tolerances) is a reasonable approach for modeling additive effects. For this case, mixture components will contribute to the response only when present in the environment at concentrations that elicit the relevant response. That is, such components do not need to be considered when present at concentrations below their toxic thresholds.
7. Potential synergistic interactions need be considered only when a synergist is present in the environment above its interaction threshold concentration. In the case of synergism, it is probably prudent to generate information on toxic interactions to ensure accurate evaluation of potential responses of the species of concern.

8. In the case of antagonism, uncertainties associated with both exposures and toxic interactions will seldom justify a quantitative modification of the effects analysis.
9. The use of uncertainty factors to compensate for the absence of information on potential interactions of mixture components is not recommended. When data are available, quantitative methods can be used to evaluate the interactions.

Interspecies Extrapolation, Surrogate Species, and Other Uncertainties

- Many difficulties are associated with the use of surrogate species to estimate risk to a species on which data are not available or cannot easily be obtained.
- An alternative approach to using a single surrogate species is to define a range of sensitivities within which the sensitivity of the species of concern could reasonably be expected to occur or a range of sensitivities that could be used to make reasoned extrapolations from species that have been tested by using inferences based on other chemicals.
- Because listed species are not inherently more sensitive to chemicals than species that are not listed, similar methods of cross-species extrapolations can be used for any ecological risk assessment and include interspecies correlation analysis and species sensitivity distributions.
- Life histories need to be considered whether one is identifying a single surrogate species or using an alternative approach. For example, if two related species have similar toxic sensitivities to a chemical but have different life histories that lead them to occupy different locations at different times, their susceptibility to the chemical could be different.
- In all cases and for all methods, quantitative uncertainty analyses should be used whenever sufficient data are available.

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Risk Characterization

Risk characterization is the final stage of an ecological risk assessment in which results of exposure and effects analyses are integrated to provide decision-makers with a risk estimate—the probability of adverse effects of exposure to a chemical stressor—and its associated uncertainty. A decision-maker does not want to make a decision on the basis of a belief that a pesticide is unlikely to yield an adverse effect and discover afterwards that it did yield an adverse effect. That is often referred to as avoiding a Type II error. For example, if the US Environmental Protection Agency (EPA) proposes registering a pesticide with a specific label use, it needs to know how much confidence there is that doing so will lead to the desired outcome, such as reduction in the abundance of the target species, and not result in jeopardy to a listed species. It is most useful if the risk estimate and its associated uncertainty are expressed in a quantitative manner—for example, “there is a $20\% \pm 10\%$ probability of a 25% reduction in the population growth rate as a result of this action.”

In addition to generating a quantitative risk estimate, risk characterization includes a narrative discussion (termed the risk description) that includes discussion of data gaps, lack of knowledge, natural variability, and other factors that might influence confidence in the risk estimate. The discussion can be viewed as a weight-of-evidence description in which the strengths and weaknesses of each assumption and each type of data used in the risk assessment are discussed. At the risk assessor’s discretion, the narrative might be summarized in a table that lists all the lines of evidence and their various weights that are scored on the basis of relevance, degree of quantification, variability, and robustness of the data analysis (see, for example, Linkov et al. 2009; Exponent 2010). The discussion provides guidance to the decision-maker about which aspects of the risk assessment are more reliable, where there are greater unknowns, and how natural variability or lack of knowledge might hinder the development of a more accurate estimate of risk.

There are many practical methods for combining the results (with their associated uncertainties) of exposure and effects analyses to provide an estimate of risk and the confidence in it. Two broad approaches have been used; one is a

deterministic concentration-ratio approach, which compares point estimates of exposure and effect concentrations, and the other is a probabilistic approach, which evaluates the probability that exposure to a chemical will lead to a specified adverse effect at some future time. The latter is technically sound, and the former is ad hoc (although commonly used) and has unpredictable performance outcomes. EPA uses the concentration-ratio approach for its assessments. In biological opinions on salmon, the National Marine Fisheries Service appears to favor a probabilistic approach that is based on population modeling. The Fish and Wildlife Service seems not to use a quantitative approach, either concentration-ratio or probabilistic, for risk characterization.

CONCENTRATION-RATIO APPROACH

The concentration-ratio approach, which is commonly used by EPA for Step 1 and 2 assessments (see Figure 2-1), does not estimate risk (the probability of an adverse effect) itself but rather relies on there being a large margin between a point estimate of the most likely maximum pesticide environmental concentration and a point estimate of the lowest concentration at which a specified adverse effect might be expected (EPA 2004). The superficial attraction of this approach is that one feels confident that a decision will not lead to an adverse effect (that is, a Type II error will be avoided) if sufficiently large margins are used. There is a belief that the larger the margin between the estimated exposure and the response threshold, the greater the certainty (or the smaller the uncertainty). The flaws in that approach are that it does not account for the probability of an adverse effect before worst-case assumptions are applied and that it does not calculate how the use of the assumptions modifies that probability. Given that approach, decision-makers do not know what the probability of an adverse effect is, but they hope that they can assume (or be reassured) that it is small. However, such an assumption is not reliable. If they or their constituencies have doubts, the common response is to widen the margin with additional conservative assumptions, including addition of specific uncertainty factors or more stringent, and possibly implausible, exposure scenarios. However, simply widening the gap indefinitely might lead to decisions that limit pesticide use to a greater extent than is intended by policy and will not meaningfully express the underlying probability of an adverse effect.

For pesticides, as evaluated by EPA, the concentration ratio is quantified in the form of a risk quotient (RQ) that might be less or greater than some specified level of concern (LOC). However, an RQ is not actually a risk estimate in that it provides no information about the probability of an adverse effect. Thus, although an RQ of 10 is several times higher than most numerical LOCs, there is no fixed relationship between RQs and the probability of an adverse effect on a listed species. Therefore, it is not possible to determine what an RQ of 10 means with respect to a possible adverse effect on a listed species. Nor is there a fixed relationship for comparing the difference between, for example, RQs of 10 and

100 with respect to the probability of an adverse effect. Theoretically, an RQ of 100 means a greater probability of an adverse effect than an RQ of 10, but one cannot determine whether the difference in probability between the two RQs is substantial or negligible or whether the final error associated with the risk estimate is appropriate for the management needs.

Thus, although RQs are often used by EPA for Step 2 assessments that might trigger later, more refined and focused assessments for listed species, the committee concludes that RQs are not appropriate for assessments for listed species or indeed for any application in which it is desired to base a decision on the probabilities of various possible outcomes. Furthermore, the committee concludes that adding uncertainty factors to RQs to account for lack of data (on formulation toxicity, synergy, additivity, or any other aspect) is unwarranted because there is no way to determine whether the assumptions being used substantially overestimate or underestimate the probability of an adverse effect.

The committee has not been asked about and is not commenting on policy decisions about what level of risk is acceptable or how conservative the agencies should be in establishing an "acceptable" risk level when considering jeopardy to listed species.

PROBABILISTIC APPROACH

Risk is defined as the probability of an adverse effect (Burmaster 1996). Thus, natural tools for quantifying and analyzing risk are probability, statistics, and the algebra of random variables, and an alternative to the deterministic concentration-ratio approach is a probabilistic one. In the probabilistic approach, the probability that a decision will lead to an adverse effect is calculated from the available information and then used to support an informed decision (again, the committee is purposefully refraining from a discussion of what an "acceptable" probability of risk might be). The probabilistic approach requires integration of the uncertainties (from sampling, natural variability, lack of knowledge, and measurement and model error) in the exposure and effects analyses by using probability distributions, rather than single point estimates, for uncertain quantities (EPA 2001). The distributions are then integrated mathematically to calculate the risk as a probability and its associated uncertainty in that estimate. Ultimately, decision-makers are provided with a risk estimate that reflects the probability of exposure to a range of pesticide concentrations and the magnitude of an adverse effect (if any) to the exposures that answers the fundamental question, What is the probability that registration of this pesticide will lead to a specified adverse effect on a listed species or its critical habitat?

Implementing a probabilistic approach requires three primary actions on the part of a risk assessor:

- (1) Describe uncertain variables with distributions and recognize that not all variables in a model or an analysis need be treated this way. The task can be

made considerably more tractable if only variables identified as key drivers via a sensitivity analysis are defined by distributions. The methods and problems in fitting or otherwise deriving the distributions from data are not discussed here because a large literature is available on these topics (see, for example, EUFRAM 2006; Warren-Hicks and Hart 2010). However, the models or measurements used to estimate exposure concentrations are capable of providing results as distributions, and results of the multispecies toxicity testing that is already part of the registration process could be expressed as discrete exposure-response distributions or combined into a species sensitivity distribution.

(2) Propagate the uncertainty through to distributions of exposure and effect by using one of several calculation methods. The most readily accessible of these (in terms of software and experience) are Monte Carlo analysis (including second-order methods), probability-bounds analysis, and Bayesian methods (Warren-Hicks and Hart 2010) (see Chapter 2 for recommendations of method selection).

(3) Integrate exposure and effect estimates to calculate risk. Aldenberg et al. (2001) have shown that a variety of risk-estimation methods calculate the same probability that a stated exposure concentration will produce a specified adverse effect given a specific exposure-response relationship. Such methods include discrete summation for expected risk (Cardwell et al. 1999), ecological risk overlap plot (Van Straalen 2002), numerical integration of risk-distribution curves (Parkhurst et al. 1996; Solomon and Takacs 2001; Warren-Hicks et al. 2001), and various area-under-the-curve (AUC) methods, such as exceedance profile plots (ECOFRAM 1999ab; Giesy et al. 1999; Solomon and Takacs 2001), cumulative profile plots (Aldenberg et al. 2001), and cumulative distribution functions of risk estimates (Aldenberg et al. 2001; EUFRAM 2006). The area under the joint probability curve is considered as a numerical measure of the risk to a species posed by a chemical stressor (Giddings et al. 2005), a value that a decision-maker would seek to minimize.

The committee has concluded that EPA and the Services can begin the transition now from concentration ratios to established, scientifically defensible statistical-inference methods for propagating uncertainties in exposure and effect through to a risk estimate for both individual receptors (Step 2) and populations of receptors (Step 3). The committee recognizes the pragmatic demands of the pesticide registration process and encourages EPA and the Services to consider probabilistic methods that have already been successfully applied to pesticide risk assessments (Odenkirchen 2003 [EPA's Terrestrial Investigation Model v 2.0]; Giddings et al 2005; Warren-Hicks and Hart 2010), have otherwise appeared frequently in the technical literature, are familiar to many risk-assessment practitioners, can be implemented with commercially available software, and are most readily explicable to decision-makers, stakeholders, and the public. The committee also notes that transitioning to a probabilistic approach can begin with simple registrations (for example, pesticides for use on a few crops or in a small geographic area) and will not require that all variables be immediately represented with prob-

ability distributions (that is, sensitivity analyses can be used to identify key parameters that are important to represent as probability distributions).

CONCLUSIONS

- Inclusion of uncertainty factors to account for lack of various data is unwarranted because there is no way to determine whether the assumptions being used substantially overestimate or underestimate the probability of adverse effects.
- RQs are not appropriate for risk assessments or for any application in which it is desired to base a decision on the probabilities of the various possible outcomes.
- EPA (for Step 2 assessments) and the Services (for Step 3 assessments) should use established, scientifically defensible, statistical methods to calculate risk as a probability to assist decision-makers' understanding of the potential consequences of their decisions.
- A number of existing probabilistic methods have been shown to be applicable and practical for ecological risk assessments that involve pesticides.
- The transition from concentration-ratio to probabilistic approaches can begin now, starting with simple registrations, focusing on a small set of sensitive key parameters, and drawing on the considerable literature and guidance on probabilistic approaches.

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Appendix A

Selected Excerpts from 40 CFR Part 158 Data Requirements for Pesticides

158.1 Purpose and scope.

a) *Purpose.* The purpose of this part is to specify the kinds of data and information EPA requires in order to make regulatory judgments under FIFRA secs. 3, 4, and 5 about the risks and benefits of pesticide products. Further, this part specifies the data and information needed to determine the safety of pesticide chemical residues under FFDCA sec. 408.

b) *Scope—*

(1) This part describes the minimum data and information EPA typically requires to support an application for pesticide registration or amendment; support the reregistration of a pesticide product; support the maintenance of a pesticide registration by means of the data call-in process, e.g., as used in the registration review program; or establish or maintain a tolerance or exemption from the requirements of a tolerance for a pesticide chemical residue.

(2) This part establishes general policies and procedures associated with the submission of data in support of a pesticide regulatory action.

(3) This part does not include study protocols, methodology, or standards for conducting or reporting test results; nor does this part describe how the Agency uses or evaluates the data and information in its risk assessment and risk management decisions, or the regulatory determinations that may be based upon the data.

* * *

§ 158.30 Flexibility.

a) FIFRA provides EPA flexibility to require, or not require, data and information for the purposes of making regulatory judgments for pesticide products. EPA has the authority to establish or modify data needs for individual pesticide chemicals. The actual data required may be modified on an individual

basis to fully characterize the use and properties, characteristics, or effects of specific pesticide products under review. The Agency encourages each applicant to consult with EPA to discuss the data requirements particular to its product prior to and during the registration process.

b) The Agency cautions applicants that the data routinely required in this part may not be sufficient to permit EPA to evaluate the potential of the product to cause unreasonable adverse effects to man or the environment. EPA may require the submission of additional data or information beyond that specified in this part if such data or information are needed to appropriately evaluate a pesticide product.

c) This part will be updated as needed to reflect evolving program needs and advances in science.

* * *

§ 158.70 Satisfying data requirements.

a) *General policy.* The Agency will determine whether the data submitted or cited to fulfill the data requirements specified in this part are acceptable. This determination will be based on the design and conduct of the experiment from which the data were derived, and an evaluation of whether the data fulfill the purpose(s) of the data requirement. In evaluating experimental design, the Agency will consider whether generally accepted methods were used, sufficient numbers of measurements were made to achieve statistical reliability, and sufficient controls were built into all phases of the experiment. The Agency will evaluate the conduct of each experiment in terms of whether the study was conducted in conformance with the design, good laboratory practices were observed, and results were reproducible. The Agency will not reject data merely because they were derived from studies which, when initiated, were in accordance with an Agency-recommended protocol, even if the Agency subsequently recommends a different protocol, as long as the data fulfill the purposes of the requirements as described in this paragraph.

(1) The provisions in this part 158 should be read in conjunction with the provisions in §152.85 to claim eligibility for the formulators' exemption.

(2) [Reserved]

b) *Good laboratory practices.* Applicants must adhere to the good laboratory practice (GLP) standards described in 40 CFR part 160 when conducting studies. Applicants must also adhere to GLP standards when conducting a study in support of a waiver request of any data requirement which is within the scope of the GLP requirements.

c) *Agency guidelines.* EPA has published Test Guidelines that contain standards for conducting acceptable tests, guidance on the evaluation and reporting of data, definition of terms, and suggested study protocols. Copies of the Test Guidelines may be obtained by visiting the agency's website at www.epa.gov/pesticides.

d) *Study protocols—*

(1) *General.* Any appropriate protocol may be used to generate the data required by this part, provided that it meets the purpose of the test standards specified in the pesticide assessment guidelines, and provides data of suitable quality and completeness as typified by the protocols cited in the guidelines. Applicants should use the test procedure which is most suitable for evaluation of the particular ingredient, mixture, or product. Accordingly, failure to follow a suggested protocol will not invalidate a test if another appropriate methodology is used.

(2) *Organization for Economic Co-Operation and Development (OECD) protocols.* Tests conducted in accordance with the requirements and recommendations of the applicable OECD protocols can be used to develop data necessary to meet the requirements specified in this part. Applicants should note, however, that certain of the OECD recommended test standards, such as test duration and selection of test species, are less restrictive than those recommended by EPA. Therefore, when using OECD protocols, care should be taken to observe the test standards in a manner such that the data generated by the study will satisfy the requirements of this part.

e) *Combining studies.* Certain toxicology studies may be combined to satisfy data requirements. For example, carcinogenicity studies in rats may be combined with the rat chronic toxicity study. Combining appropriate studies may be expected to reduce usage of test animals as well as reduce the cost of studies. EPA encourages this practice by including standards for acceptable combined tests in the Pesticide Assessment Guidelines. Registrants and applicants are encouraged to consider combining other tests when practical and likely to produce scientifically acceptable results. Registrants and applicants, however, must consult with the EPA before initiating combined studies.

* * *

§ 158.75 Requirements for additional data.

The data routinely required by this part may not be sufficient to permit EPA to evaluate every pesticide product. If the information required under this part is not sufficient to evaluate the potential of the product to cause unreasonable adverse effects on man or the environment, additional data requirements will be imposed. However, EPA expects that the information required by this part will be adequate in most cases for an assessment of the properties and effects of the pesticide.

§ 158.80 Use of other data.

a) *Data developed in foreign countries.* With certain exceptions, laboratory and field study data developed outside the United States may be submitted in support of a pesticide registration. Data generated in a foreign country which the

Agency will not consider include, but are not limited to, data from tests which involved field test sites or a test material, such as a native soil, plant, or animal, that is not characteristic of the United States. Applicants submitting foreign data must take steps to ensure that U.S. materials are used, or be prepared to supply data or information to demonstrate the lack of substantial or relevant differences between the selected material or test site and the U.S. material or test site. Once submitted, the Agency will determine whether or not the data meet the data requirements.

b) *Data generated for other purposes.* Data developed for purposes other than satisfaction of FIFRA data requirements, such as monitoring studies, may also satisfy data requirements in this part. Consultation with the Agency should be arranged if applicants are unsure about suitability of such data.

* * *

§ 158.130 Purposes of the registration data requirements.

e) *Hazards to nontarget organisms—*

(1) *General.* The information required to assess hazards to nontarget organisms is derived from tests to determine pesticidal effects on birds, mammals, fish, terrestrial and aquatic invertebrates and plants. These tests include short-term acute, subacute, reproduction, simulated field, and full field studies arranged in a hierarchical or tier system which progresses from the basic laboratory tests to the applied field tests. The results of each tier of testing must be evaluated to determine the potential of the pesticide to cause adverse effects, and to determine whether further testing is required. A purpose common to all data requirements is to provide data which determine the need for (and appropriate wording for) precautionary label statements to minimize the potential adverse effects to nontarget organisms.

(2) *Short-term studies.* The short-term acute and subchronic laboratory studies provide basic toxicity information which serves as a starting point for the hazard assessment. These data are used: To establish acute toxicity levels of the active ingredient to the test organisms; to compare toxicity information with measured or estimated pesticide residues in the environment in order to assess potential impacts on fish, wildlife and other nontarget organisms; and to indicate whether further laboratory and/or field studies are needed.

(3) *Long-term and field studies.* Additional studies (*i.e.*, avian, fish, and invertebrate reproduction, life cycle studies and plant field studies) may be required when basic data and environmental conditions suggest possible problems. Data from these studies are used to: Estimate the potential for chronic effects, taking into account the measured or estimated residues in the environment; and to determine if additional field or laboratory data are necessary to further evaluate hazards. Simulated field and/or field data are used to examine acute and chronic adverse effects

on captive or monitored fish and wildlife populations under natural or near-natural environments. Such studies are required only when predictions as to possible adverse effects in less extensive studies cannot be made, or when the potential for adverse effects is high.

* * *

g) *Pesticide spray-drift evaluation.* Data required to evaluate pesticide spray drift are derived from studies of droplet size spectrum and spray drift field evaluations. These data contribute to the development of the overall exposure estimate and, along with data on toxicity for humans, fish and wildlife, or plants, are used to assess the potential hazard of pesticides to these organisms. A purpose common to all these tests is to provide data which will be used to determine the need for (and appropriate wording for) precautionary labeling to minimize the potential adverse effect to nontarget organisms.

h) *Environmental fate—*

(1) *General.* The data generated by environmental fate studies are used to: Assess the toxicity to man through exposure of humans to pesticide residues remaining after application, either upon reentering treated areas or from consuming inadvertently-contaminated food; assess the presence of widely distributed and persistent pesticides in the environment which may result in loss of usable land, surface water, ground water, and wildlife resources; and, assess the potential environmental exposure of other nontarget organisms, such as fish and wildlife, to pesticides. Another specific purpose of the environmental fate data requirements is to help applicants and the Agency estimate expected environmental concentrations of pesticides in specific habitats where threatened or endangered species or other wildlife populations at risk are found.

(2) *Degradation studies.* The data from hydrolysis and photolysis studies are used to determine the rate of pesticide degradation and to identify pesticides that may adversely affect nontarget organisms.

(3) *Mobility studies.* These data requirements pertain to leaching, adsorption/desorption, and volatility of pesticides. They provide information on the mode of transport and eventual destination of the pesticide in the environment. This information is used to assess potential environmental hazards related to: Contamination of human and animal food; loss of usable land and water resources to man through contamination of water (including ground water); and habitat loss of wildlife resulting from pesticide residue movement or transport in the environment.

* * *

(4) *Accumulation studies.* Accumulation studies indicate pesticide residue levels in food supplies that originate from wild sources or from rotational crops. Rotational crop studies are necessary to establish realistic crop rotation restrictions and to determine if tolerances may be

needed for residues on rotational crops. Data from irrigated crop studies are used to determine the amount of pesticide residues that could be taken up by representative crops irrigated with water containing pesticide residues. These studies allow the Agency to establish label restrictions regarding application of pesticides on sites where the residues can be taken up by irrigated crops. These data also provide information that aids the Agency in establishing any corresponding tolerances that would be needed for residues on such crops. Data from pesticide accumulation studies in fish are used to establish label restrictions to prevent applications in certain sites so that there will be minimal residues entering edible fish or shellfish. These residue data are also used to determine if a tolerance or action level is needed for residues in aquatic animals eaten by humans.

* * *

Subpart G – Ecological Effects

§ 158.630 Terrestrial and aquatic nontarget organisms data requirements table.

a) *General.* Sections 158.100 through 158.130 describe how to use this table to determine the terrestrial and aquatic nontarget data requirements for a particular pesticide product. Notes that apply to an individual test including specific conditions, qualifications, or exceptions to the designated test are listed in paragraph (e) of this section.

b) *Use patterns.*

(1) The terrestrial use pattern includes products classified under the general use patterns of terrestrial food crop, terrestrial feed crop, and terrestrial nonfood crop. The aquatic use pattern includes products classified under the general use patterns of aquatic food crop and aquatic nonfood use patterns. The greenhouse use pattern includes products classified under the general use patterns of greenhouse food crop and greenhouse nonfood crop. The indoor use pattern includes products classified under the general use patterns of indoor food and indoor nonfood use.

(2) Data are also required for the general use patterns of forestry and residential outdoor use.

(3) In general, for all outdoor end-uses, including turf, the following studies are required: Two avian oral LD₅₀, two avian dietary LC₅₀, two avian reproduction studies, two freshwater fish LC₅₀, one freshwater invertebrate EC₅₀, one honeybee acute contact LD₅₀, one freshwater fish early-life stage, one freshwater invertebrate life cycle, and three estuarine acute LC₅₀/EC₅₀ studies—fish, mollusk and invertebrate. All other outdoor residential uses, *i.e.*, gardens and ornamental will not usually require the freshwater fish early-life stage, the freshwater invertebrate life-cycle, and the acute estuarine tests.

c) *Key.* R = Required; CR = Conditionally required; NR = Not required; TGAI = Technical grade of the active ingredient; TEP = Typical end-use product; PAI = Pure active ingredient; EP = end-use product. Commas between the test substances (*i.e.*, TGAI, TEP) indicate that data may be required on the TGAI or the TEP depending on the conditions set forth in the test note.

d) *Table.* The following table shows the data requirements for nontarget terrestrial and aquatic organism. The table notes are shown in paragraph (e) of this section.

e) *Test notes.* The following test notes apply to terrestrial and aquatic nontarget organisms data requirements in the table to paragraph (d) of this section:

(1) Data using the TGAI are required to support all outdoor end-use product uses including, but not limited to turf. Data are generally not required to support end-use products in the form of a gas, a highly volatile liquid, a highly reactive solid, or a highly corrosive material.

(2) For greenhouse and indoor end-use products, data using the TGAI are required to support manufacturing-use products to be reformulated into these same end-use products or to support end-use products when there is no registered manufacturing-use product. Avian acute oral data are not required for liquid formulations for greenhouse and indoor uses. The study is not required if there is no potential for environmental exposure.

(3) Data are required on one passerine species and either one waterfowl species or one upland game bird species for terrestrial, aquatic, forestry, and residential outdoor uses. Data are preferred on waterfowl or upland game bird species for indoor and greenhouse uses.

(4) Data are required on waterfowl and upland game bird species.

(5) Tests are required based on the results of lower tier toxicology studies, such as the acute and subacute testing, intended use pattern, and environmental fate characteristics that indicate potential exposure.

(6) Higher tier testing may be required for a specific use pattern when a refined risk assessment indicates a concern based on laboratory toxicity endpoints and refined exposure assessments.

(7) Environmental chemistry methods used to generate data associated with this study must include results of a successful confirmatory method trial by an independent laboratory. Test standards and procedures for independent laboratory validation are available as addenda to the guideline for this test requirement.

(8) Data are required on one coldwater fish and one warmwater fish for terrestrial, aquatic, forestry, and residential outdoor uses. For indoor and greenhouse uses, testing with only one of either fish species is required.

Terrestrial and Aquatic Nontarget Organism Data Requirements

Guideline Number	Data Requirement	Use Pattern						Test substance	Test Note No.
		Terrestrial	Aquatic	Forestry	Residential Outdoor	Greenhouse	Indoor		
Avian and Mammalian Testing									
850.2100	Avian oral toxicity	R	R	R	R	CR	CR	TGA1	1, 2, 3
850.2200	Avian dietary toxicity	R	R	R	R	NR	NR	TGA1	1, 4
850.2400	Wild mammal toxicity	CR	CR	CR	CR	NR	NR	TGA1	5
850.2300	Avian reproduction	R	R	R	R	NR	NR	TGA1	1, 4
850.2500	Simulated or actual field testing	CR	CR	CR	CR	NR	NR	TEP	6, 7
Aquatic Organisms Testing									
850.1075	Freshwater fish toxicity	R	R	R	R	CR	CR	TGA1, TEP	1, 2, 8, 9, 26
850.1010	Acute toxicity freshwater invertebrates	R	R	R	R	CR	CR	TGA1, TEP	1, 2, 9, 10, 26
850.1025 850.1035 850.1045 850.1055 850.1075	Acute toxicity estuarine and marine organisms	R	R	R	R	NR	NR	TGA1, TEP	1, 9, 11, 12, 26
850.1300	Aquatic invertebrate life cycle (freshwater)	R	R	R	R	NR	NR	TGA1	1, 10, 12
850.1350	Aquatic invertebrate life cycle (saltwater)	CR	CR	CR	CR	NR	NR	TGA1	12, 14, 15
850.1400	Fish early-life stage (freshwater)	R	R	R	R	NR	NR	TGA1	1, 12, 13
850.1400	Fish early-life stage (saltwater)	CR	CR	CR	CR	NR	NR	TGA1	12, 15, 16
850.1500	Fish life cycle	CR	CR	CR	CR	NR	NR	TGA1	17, 18

850.1710 850.1730 850.1850	Aquatic organisms bioavailability, biomagnification, toxicity	CR	CR	CR	CR	NR	NR	TGAI, PAI, degradate	19
850.1950	Simulated or actual field testing for aquatic organisms	CR	CR	CR	CR	NR	NR	TEP	7, 20
Sediment Testing									
850.1735	Whole sediment: acute freshwater invertebrates	CR	CR	CR	CR	NR	NR	TGAI	21
850.1740	Whole sediment: acute marine invertebrates	CR	CR	CR	CR	NR	NR	TGAI	21, 23
	Whole sediment: chronic invertebrates freshwater and marine	CR	CR	CR	CR	NR	NR	TGAI	22, 23
Insect Pollinator Testing									
850.3020	Honeybee acute contact toxicity	R	CR	R	R	NR	NR	TGAI	1
850.3030	Honey bee toxicity of residues on foliage	CR	CR	CR	CR	NR	NR	TEP	24
850.3040	Field testing for pollinators	CR	CR	CR	CR	NR	NR	TEP	25

(9) EP or TEP testing is required for any product which meets any of the following conditions:

- i. The end-use pesticide will be introduced directly into an aquatic environment (e.g., aquatic herbicides and mosquito larvicides) when used as directed.
- ii. The maximum expected environmental concentration (MEEC) or the estimated environmental concentration (EEC) in the aquatic environment is \geq one-half the LC_{50} or EC_{50} of the TGAI when the EP is used as directed.
- iii. An ingredient in the end-use formulation other than the active ingredient is expected to enhance the toxicity of the active ingredient or to cause toxicity to aquatic organisms.

(10) Data are required on one freshwater aquatic invertebrate species.

(11) Data are required on one estuarine/marine mollusk, one estuarine/marine invertebrate and one estuarine/marine fish species.

(12) Data are generally not required for outdoor residential uses, other than turf, unless data indicate that pesticide residues from the proposed use(s) can potentially enter waterways.

(13) Data are required on one freshwater fish species. If the test species is different from the two species used for the freshwater fish acute toxicity tests, a 96-hour LC_{50} on that species must also be provided.

(14) Data are required on one estuarine/marine invertebrate species.

(15) Data are required on estuarine/marine species if the product meets any of the following conditions:

- i. Intended for direct application to the estuarine or marine environment.
- ii. Expected to enter this environment in significant concentrations because of its expected use or mobility patterns.
- iii. If the acute LC_{50} or $EC_{50} < 1$ milligram/liter (mg/l).
- iv. If the estimated environmental concentration (EEC) in water is ≥ 0.01 of the acute EC_{50} or LC_{50} or if any of the following conditions exist:
 - A. Studies of other organisms indicate the reproductive physiology of fish and/or invertebrates may be affected.
 - B. Physicochemical properties indicate bioaccumulation of the pesticide.
 - C. The pesticide is persistent in water (e.g., half-life in water > 4 days).

(16) Data are required on one estuarine/marine fish species.

(17) Data are required on estuarine/marine species if the product is intended for direct application to the estuarine or marine environment, or the product is expected to enter this environment in significant concentrations because of its expected use or mobility patterns.

(18) Data are required on freshwater species if the end-use product is intended to be applied directly to water, or is expected to be transported

to water from the intended use site, and when any of the following conditions apply:

- i. If the estimated environmental concentration (EEC) is ≥ 0.1 of the no-observed-effect level in the fish early-life stage or invertebrate life cycle test;
- ii. If studies of other organisms indicate that the reproductive physiology of fish may be affected.

(19) Not required when:

- i. The octanol/water partition coefficients of the pesticide and its major degradates are $< 1,000$; or
- ii. There are no potential exposures to fish and other nontarget aquatic organisms; or
- iii. The hydrolytic half-life is < 5 days at pH 5, 7 and 9.

(20) Data are required based on the results of lower tier studies such as acute and chronic aquatic organism testing, intended use pattern, and environmental fate characteristics that indicate significant potential exposure.

(21) Data are required if:

- i. The half-life of the pesticide in the sediment is ≤ 10 days in either the aerobic soil or aquatic metabolism studies and if any of the following conditions exist:

- A. The soil partition coefficient (K_d) is ≥ 50 .
- B. The log K_{ow} is ≥ 3 .
- C. The $K_{oc} \geq 1,000$.

- ii. Registrants must consult with the Agency on appropriate test protocols prior to designing the study.

(22) Data are required if:

- i. The estimated environmental concentration (EEC) in sediment is > 0.1 of the acute LC_{50}/EC_{50} values and
- ii. The half-life of the pesticide in the sediment is > 10 days in either the aerobic soil or aquatic metabolism studies and if any of the following conditions exist:

- A. The soil partition coefficient (K_d) is ≥ 50 .
- B. The log K_{ow} is ≥ 3 .
- C. The $K_{oc} \geq 1,000$.

- iii. Registrants must consult with the Agency on appropriate test protocols prior to designing the study.

(23) Sediment testing with estuarine/marine test species is required if the product is intended for direct application to the estuarine or marine environment or the product is expected to enter this environment in concentrations which the Agency believes to be significant, either by runoff or erosion, because of its expected use or mobility pattern.

(24) Data are required only when the formulation contains one or more active ingredients having an acute LD_{50} of < 11 micrograms per bee as

determined in the honey bee acute contact study and the use pattern(s) indicate(s) that honey bees may be exposed to the pesticide.

(25) Required if any of the following conditions are met:

- i. Data from other sources (Experimental Use Permit program, university research, registrant submittals, etc.) indicate potential adverse effects on colonies, especially effects other than acute mortality (reproductive, behavioral, etc.);
- ii. Data from residual toxicity studies indicate extended residual toxicity.
- iii. Data derived from studies with terrestrial arthropods other than bees indicate potential chronic, reproductive or behavioral effects.

(26) The freshwater fish test species for the TEP testing is the most sensitive of the species tested with the TGAI. Freshwater invertebrate and acute estuarine and marine organisms must also be tested with the EP or TEP using the same species tested with the TGAI.

* * *

Subpart L – Spray Drift

§ 158.1100 Spray drift data requirements table.

a) *General.* Sections 158.100 through 158.130 describe how to use this table to determine the spray drift data requirements for a particular pesticide product. Notes that apply to an individual test, including specific conditions, qualifications, or exceptions to the designated test are listed in paragraph (e) of this section.

b) *Use patterns.* The terrestrial use pattern includes products classified under the general use patterns of terrestrial food crop and terrestrial nonfood crop. The aquatic use pattern includes products classified under the general use patterns of aquatic food crop and aquatic nonfood. The greenhouse use pattern includes products classified under the general use patterns of greenhouse food crop and greenhouse nonfood crop. Data are also required for the general use patterns of forestry use, residential outdoor use, and indoor use.

c) *Key.* CR = Conditionally required; NR = Not required; TEP = Typical end-use product; MP = Manufacturing use product; EP = End-use product.

d) *Table.* The following table lists the data requirements that pertain to spray drift. The table notes are shown in paragraph (e) of this section.

* * *

Subpart N – Environmental Fate

§ 158.1300 Environmental fate data requirements table.

a) *General.* All environmental fate data, as described in paragraph (c) of this section, must be submitted to support a request for registration.

b) *Use patterns.*

(1) The terrestrial use pattern includes products classified under the general use patterns of terrestrial food crop, terrestrial feed crop, and terrestrial nonfood. The aquatic use pattern includes the general use patterns of aquatic food crop, and aquatic nonfood. The greenhouse use pattern includes both food and nonfood uses. The indoor use pattern includes food, nonfood, and residential indoor uses.

(2) Data are also required for the general use patterns of forestry use and residential outdoor use.

c) *Key*. CR = Conditionally required; NR = Not required; R = Required; PAIRA = Pure active ingredient radio-labeled; TGAI = Technical grade of the active ingredient; TEP = Typical end-use product.

d) *Table*. The following table shows the data requirements for environmental fate. The test notes are shown in paragraph (e) of this section.

e) *Test notes*. The following test notes apply to the requirements in the table to paragraph (d) of this section:

(1) Study is required for indoor uses in cases where environmental exposure is likely to occur. Such sites include, but are not limited to, agricultural premises, in or around farm buildings, barnyards, and beehives.

(2) Not required when the electronic absorption spectra, measured at pHs 5, 7, and 9, of the chemical and its hydrolytic products, if any, show no absorption or tailing between 290 and 800 nm.

(3) Not required when the chemical is to be applied only by soil injection or is incorporated in the soil.

(4) Requirement based on use patterns and other pertinent factors including, but not limited to, the Henry's Law Constant of the chemical. In view of methodological difficulties with the study of photodegradation in air, prior consultation with the Agency regarding the protocol is recommended before the test is performed.

(5) Required for aquatic food and nonfood crop uses for aquatic sites that are intermittently dry. Such sites include, but are not limited to, cranberry bogs and rice paddies.

(6) Adsorption and desorption using a batch equilibrium method is preferred. However in some cases, for example, where the pesticide degrades rapidly, soil column leaching with unaged or aged columns may be more appropriate to fully characterize the potential mobility of the parent compound and major transformation products.

(7) Environmental chemistry methods used to generate data associated with this study must include results of a successful confirmatory method trial by an independent laboratory. Test standards and procedures for independent laboratory validation are available as addenda to the guideline for this test requirement.

(8) Requirement for terrestrial uses is based on potential for aquatic exposure and if pesticide residues have the potential for persistence, mobility, nontarget aquatic toxicity or bioaccumulation. Not required for aquatic residential uses. Field testing under the terrestrial field dissipa-

tion requirement may be more appropriate for some aquatic food crops, such as rice and cranberry uses, that are managed to have a dry-land period for production. The registrant is encouraged to consult with the Agency on protocols.

(9) Agency approval of a protocol is necessary prior to initiation of the study.

(10) This study may be triggered if there is specific evidence that the presence of one pesticide can affect the dissipation characteristics of another pesticide when applied simultaneously or serially.

(11) Required if the weight-of-evidence indicates that the pesticide and/or its degradates is likely to leach to ground water, taking into account other factors such as the toxicity of the chemicals(s), available monitoring data, and the vulnerability of ground water resources in the pesticide use area.

(12) If the terrestrial dissipation study cannot assess all of the major routes of dissipation, the forestry.

Table—Spray Drift Data Requirements

Guideline Number	Data Requirement	Use Pattern									Test substance		Test Note No.
		Terrestrial		Aquatic		Greenhouse		Forestry	Residential Outdoor	Indoor	MP	EP	
		Food Crop	Nonfood Crop	Food	Nonfood	Food Crop	Nonfood Crop						
201-1	Droplet size spectrum	CR	CR	CR	CR	NR	NR	CR	NR	NR	TEP	TEP	1
202-1	Droplet size spectrum	CR	CR	CR	CR	NR	NR	CR	NR	NR	TEP	TEP	1

e) *Test notes.* The following notes apply to the requirements in the table to paragraph (d) of this section:

(1) This study is required when aerial applications (rotary and fixed winged) and mist blower or other methods of ground application are proposed and it is estimated that the detrimental effect level of those nontarget organisms expected to be present would be exceeded. The nontarget organisms include humans, domestic animals, fish and wildlife, and nontarget plants.

Table—Environmental Fate Data Requirements

Guideline Number	Data Requirement	Use Pattern						Test substance	Test Note No.
		Terrestrial	Aquatic	Greenhouse	Indoor	Forestry	Residential Outdoor		
Degradation Studies - Laboratory									
835.2120	Hydrolysis	R	R	R	CR	R	R	TGAI or PAIRA	1
835.2240	Photodegradation in water	R	R	NR	NR	R	NR	TGAI or PAIRA	2
835.2410	Photodegradation on soil	R	NR	NR	NR	R	NR	TGAI or PAIRA	3
835.2370	Photodegradation in air	CR	NR	CR	NR	CR	CR	TGAI or PAIRA	4
Metabolism Studies - Laboratory									
835.4100	Aerobic soil	R	CR	R	NR	R	R	TGAI or PAIRA	5
835.4200	Anaerobic soil	R	NR	NR	NR	NR	NR	TGAI or PAIRA	--
835.4300	Aerobic aquatic	R	R	NR	NR	R	NR	TGAI or PAIRA	--
835.4400	Anaerobic aquatic	R	R	NR	NR	R	NR	TGAI or PAIRA	--
Mobility Studies									
835.1230 835.1240	Leaching and adsorption/desorption	R	R	R	NR	R	R	TGAI or PAIRA	6
835.1410	Volatility - laboratory	CR	NR	CR	NR	NR	NR	TEP	4
835.8100	Volatility - field	CR	NR	CR	NR	NR	NR	TEP	--
Dissipation Studies - Field									
835.6100	Terrestrial	R	CR	NR	NR	CR	R	TEP	5, 7, 12
835.6200	Aquatic (sediment)	CR	R	NR	NR	NR	NR	TEP	7, 8
835.6300	Forestry	NR	NR	NR	NR	CR	NR	TEP	7, 9, 12
835.6400	Combination and tank mixes	CR	CR	NR	NR	NR	NR	TEP	10
Ground Water Monitoring									
835.7100	Ground water monitoring	CR	NR	NR	NR	CR	CR	TEP	7, 9, 11

Appendix B

Biographical Information on the Committee on Ecological Risk Assessment under FIFRA and ESA

Judith E. McDowell (*Chair*) is a senior scientist and former Biology Department chair at Woods Hole Oceanographic Institution. Her research interests include physiological ecology of marine animals, developmental and energetic strategies of marine animals, physiological effects of pollutants on marine animals, and invertebrate nutrition. She has served on several National Research Council committees, including the Committee on Oil in the Sea: Phase I—Update of Inputs and the Committee on Research and Peer Review in EPA. Dr. McDowell earned a PhD in zoology from the University of New Hampshire.

H. Resit Akcakaya is a professor in the Department of Ecology and Evolution at Stony Brook University. His research focuses on methods and approaches for assessing the vulnerability of species to extinction, evaluating the effects of landscape dynamics on species persistence, projecting human land use on the basis of human population trends, and predicting the vulnerability of species to global climate change. He worked as a senior scientist at Applied Biomathematics, where he was one of the principal architects of the RAMAS library of software and developed models for risk assessment and modeling of metapopulations, for integrating metapopulation dynamics with geographic information systems, and for incorporating uncertainty into International Union for Conservation of Nature (IUCN) criteria for threatened species. Dr. Akcakaya has also been involved in practical and theoretical research on problems of species conservation, including several population-viability analysis studies. He has over 100 publications in conservation biology and theoretical ecology, including four books, and is a coauthor of two widely used textbooks (*Risk Assessment in Conservation Biology* and *Applied Population Ecology*). In addition, Dr. Akcakaya serves on the editorial boards of *Conservation Biology* and *Population Ecology* and is chair of the IUCN Red List Standards and Petitions Subcommittee. Dr.

Akcakaya earned a PhD in ecology and evolution from the State University of New York at Stony Brook.

Mary Jane Angelo is professor of law and director of the Environmental and Land Use Law Program at the University of Florida's Levin College of Law. Her research focuses on environmental law, water law, agricultural law, pesticide law, endangered species law, biotechnology law, and the integration of law and science. Before joining the faculty, Ms. Angelo served as an attorney in the US Environmental Protection Agency's Office of General Counsel and as senior assistant general counsel for the St. Johns River Water Management District. In addition, she has served on the National Research Council Committee on Independent Scientific Review of Everglades Restoration Progress. Ms. Angelo earned an MS in entomology and JD from the University of Florida.

Patrick Durkin is cofounder and principal scientist of Syracuse Environmental Research Associates, a small business engaged in chemical and biological risk assessment and documentation. He has been responsible for developing safety evaluations for chemical and biological agents on the basis of a synthesis of toxicological data, environmental persistence, and exposure estimates. Dr. Durkin has conducted numerous risk assessments and risk assessment method development tasks for the US Department of Agriculture, the US Environmental Protection Agency, and the Centers for Disease Control and Prevention Agency for Toxic Substances and Disease Registry. Dr. Durkin earned a PhD in environmental and forest zoology from SUNY College of Environmental Science and Forestry.

Erica Fleishman is a researcher in the John Muir Institute of the Environment at the University of California, Davis. Her research focuses on integration of conservation science with management and policy, especially in the intermountain western United States and California. Her work focuses on predictive modeling of occupancy and faunal responses to changes in climate, land cover, land use, and connectivity. Dr. Fleishman is a coauthor of curricula in applications of remote sensing to environmental sciences and ecological modeling. She has convened multidisciplinary teams to analyze and synthesize concepts and data on diverse topics and has facilitated or advised on the science process for multiple habitat conservation plans and natural community conservation plans in California. Dr. Fleishman is past editor in chief of *Conservation Biology* and serves on the editorial boards of *Global Ecology*, *Biogeography*, and *Ecography*. Dr. Fleishman earned a PhD in ecology, evolution, and conservation biology from the University of Nevada, Reno.

Anne Fairbrother is a principal scientist for Exponent's ecosciences practice. She has more than 30 years of experience in ecotoxicology, wildlife toxicology, contaminated-site assessment, and regulatory science for existing and emerging chemicals in the United States and Europe. Dr. Fairbrother has participated in or

led the development of guidance documents for ecological risk assessments, such as the US Environmental Protection Agency's (EPA) *Framework for Metals Risk Assessment*, the British Columbia Ministry of Environment's guidance for implementing Tier 1 ecological risk assessments of contaminated sites, and EPA's ecological soil screening levels. Recently, she served on a science advisory panel for the state of Utah and as a consultant to the British Columbia Ministry of Environment to set site-specific water-quality standards for selenium that protect fish and wildlife. Dr. Fairbrother has served as president of the Society of Environmental Toxicology and Chemistry, the American Association of Wildlife Veterinarians, and the Wildlife Disease Association. In addition, she has been a member of the National Research Council's Committee on Animals as Monitors of Environmental Hazards. Dr. Fairbrother earned a DVM from the University of California, Davis and a PhD in veterinary science from the University of Wisconsin-Madison.

Daniel Goodman was a professor of ecology at Montana State University. His research interests included environmental statistics, risk analysis, population dynamics, and environmental modeling. Dr. Goodman was a member of the Silvery Minnow PVA Working Group (Middle Rio Grande Endangered Species Collaborative), the Fish Passage Center Oversight Board of the Northwest Power and Conservation Council, the Hawaiian Monk Seal Recovery Team, and the Cook Inlet Beluga Whale Recovery Team. Dr. Goodman earned a PhD in zoology from Ohio State University.

William L. Graf is University Foundation Distinguished Professor Emeritus of the Department of Geography of the University of South Carolina and Regents Professor Emeritus in Geography at Arizona State University. His research interests include fluvial geomorphology and hydrology and policy for public land and water with an emphasis on river channel and habitat change, human effects on rivers, contaminant transport and storage in rivers, and the downstream effects of large dams. He has served as a science-policy adviser on more than 40 committees for federal, state, and local agencies and organizations. In addition, Dr. Graf has chaired and been a member of many National Research Council committees, including those focused on the Klamath River, the Platte River, the Everglades, the Missouri River, and watershed management. He is chair of the NRC Geographical Sciences Committee, a national associate of the National Academy of Sciences, and a fellow of the American Association for the Advancement of Science. Dr. Graf earned his PhD in physical geography from the University of Wisconsin-Madison with a certificate in water-resources management.

Philip M. Gschwend is a professor of civil and environmental engineering at the Massachusetts Institute of Technology. His research interests are environmental organic chemistry, phase exchanges and transformation processes, modeling fates of organic pollutants, roles of colloids and black carbons, and passive

sampling for site evaluation. The overall objective of his research is to develop means of predicting the fate of organic chemicals in natural and engineered environments. His research includes the study of such processes as sorption, air-water exchange, and biodegradation. In addition, Dr. Gschwend conducts field observations in water and sediments of groundwater, lakes, estuaries, and the ocean to validate the predictions. Dr. Gschwend earned a PhD in geochemistry from the Woods Hole Oceanographic Institution.

Bruce K. Hope is a principal environmental scientist with CH2M HILL. His expertise includes preparation and review of human, ecological, and probabilistic risk assessments; exposure modeling; development of air-toxics benchmarks; identification and management of persistent and bioaccumulative chemicals; and evaluation and communication of health and environmental risks associated with chemical releases. Dr. Hope has served on a number of US Environmental Protection Agency (EPA) Science Advisory Board committees, including that on Ecological Risk Assessment—An Evaluation of the State-of-the-Practice and EPA's Regulatory Environmental Modeling Guidance Advisory Panel. In addition, he was a member of the National Research Council Committee on Improving Risk Analysis Approaches Used by the U.S. EPA. Dr. Hope earned a PhD in biology from the University of Southern California.

Gerald A. LeBlanc is the head of and a professor in the Department of Environmental and Molecular Toxicology of North Carolina State University. His research interests include environmental signaling, sex determination and differentiation, and toxicity assessment of chemical mixtures. Dr. LeBlanc has been a member of the Executive Committee of the Research Triangle Environmental Health Collaborative, of the FIFRA National Science Advisory Panel on the potential for atrazine to affect amphibian gonadal development, and of the National Institute of Environmental Health Sciences Expert Panel on Hazards of Bisphenol A to Humans and the Environment. Dr. LeBlanc earned a PhD in biology from the University of South Florida.

Thomas P. Quinn is a professor in the School of Aquatic and Fishery Sciences of the University of Washington. His research interests focus on the behavior, ecology, evolution, and conservation of salmon, trout, and related fishes. Dr. Quinn's research blends a variety of approaches, including tagging, telemetry, direct observations, and laboratory experiments. He is studying the patterns of spawning-site selection and reproductive behavior of salmon, movements and migration patterns, evolutionary adaptations of salmon to their environments, and predator-prey ecology. He has served on the National Research Council Committee on Protection and Management of Pacific Northwest Anadromous Salmonids. Dr. Quinn earned a PhD in fisheries from the University of Washington.

Nu-May Ruby Reed recently retired as a staff toxicologist with the California Environmental Protection Agency (Cal/EPA) Department of Pesticide Regulation, where she was the lead scientist on risk-assessment issues. Her research interests were evaluating health risks posed by and developing risk-assessment guidelines on pesticides. She has been on several Cal/EPA working groups that initiate, research, and revise risk-assessment guidelines and policies, and she represented her department in task forces on community concerns and emergency response, risk-management guidance, and public education. Dr. Reed has been a member of several National Research Council Committees, including the Committee on Risk Analysis and Reviews, and is a current member of the Committee on Acute Exposure Guideline Levels. Dr. Reed earned a PhD in plant physiology from the University of California, Davis.

